rec.
25.4.80

CUK-H06059-8-P25843

Volume 53 Number 62
January 198

(8)

THE BRITISH JOURNAL OF RADIOLOGY

[illegible]
Radiation oncology
Nuclear medicine
Ultrasound
Radiological physics
Radiobiology
Radiation protection
and related disciplines

Published b
The British Institute of Radiolog

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:
D. K. BEWLEY, M.A., PH.D. F. STARER, F.R.C.P., F.R.C.R.

The Deputy Editors:
B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
J. ROYLANCE, F.R.C.R.
and
The Associate Editors:

A. B. AYERS, M.D., D.M.R.D., F.R.C.R.
THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C), F.R.C.R.
N. E. GILLIES, B.SC., PH.D.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
C. R. HILL, B.A., PH.D., D.SC., M.I.E.E., F.INST.P.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
R. W. STANFORD, M.A., F.INST.P. (Australia)
D. M. TAYLOR, D.SC., C. CHEM., F.R.I.C. (Continental Europe)

Managing Editor: MRS. LEE SURRY

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Hilary Cook, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free, payable in advance) £46·00 per annum (monthly) (U.S.A. $100.30) Single copies: £5·00.

Second class postage paid at New York. Mailing agents: N.Y. Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York, N.Y. 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

P25843

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01–935 6237 and 01–935 6867. Cable Address: "Britology, London W.1."

President: N. G. TROTT, B.SC., PH.D., F.INST.P.
Hon. Secretaries:
W. HATELY, M.B., CH.B., F.R.C.P.E., F.R.C.R., D.M.R.D. S. B. FIELD, B.SC., PH.D.
Hon. Treasurer: D. T. KERRISK

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1980

NEW ESSENTIAL IN EVERY DEPARTMENT OF RADIOLOGY

NUCLEAR MEDICINE

A Clinical Introduction

Michael Maisey

144 pages 8¼ × 11 inches 69 colour figs 280 black and white figs

Price: £9.95, post and packing free

Contents

Foreword

1. Introduction 2. Liver and Spleen Scanning 3. Brain Scanning 4. Nuclear Cardiology
5. Imaging the Skeleton with Radionuclides 6. Ventilation Perfusion Lung Scanning 7. Renal Scanning
8. Radionuclide Thyroid Scanning 9. Radionuclide Investigations in Paediatrics 10. Other Scanning Techniques

Index

Nuclear medicine is a growing specialty. In the UK alone, 20 new departments have been set up over the last decade and a similar pattern is seen throughout the developed world. Despite this growth there is a lack of practical guidebooks on the subject. The new *Nuclear Medicine — A Clinical Introduction* attempts to solve this problem.

For those outside the nuclear medicine department the book shows how nuclear medicine techniques can be used to solve clinical problems quickly and accurately. It outlines the procedures involved, describes the results obtained and then touches on ways in which radionuclides can be used in the management of disease. It will be of use to a wide range of readers — certainly to radiologists and hospital physicists but also to all those who are likely to refer patients to the nuclear medicine department.

For those already inside the nuclear medicine department the book does not purport to be an exhaustive treatise on the subject but could provide a useful basis for a teaching programme. With this in mind, the text is written clearly and systematically and is accompanied by numerous scans, function studies and colour photographs.

This new Update title will be of immense value to all those who want to learn about (or to teach) nuclear medicine and the benefits it offers in diagnosis and treatment.

UPDATE BOOKS

Send your order and remittance to
Book Sales Dept, Update Books
Ltd, 33 to 34 Alfred Place,
London WC1E 7DP. The
book will reach you
within 28 days.

I wish to purchase ...... copies of 'Nuclear Medicine — A Clinical Introduction' by Michael Maisey at £9.95, p. & p. free.

I enclose cheque/PO for £ .... made payable to Update Books Ltd.

NAME (block caps) ....

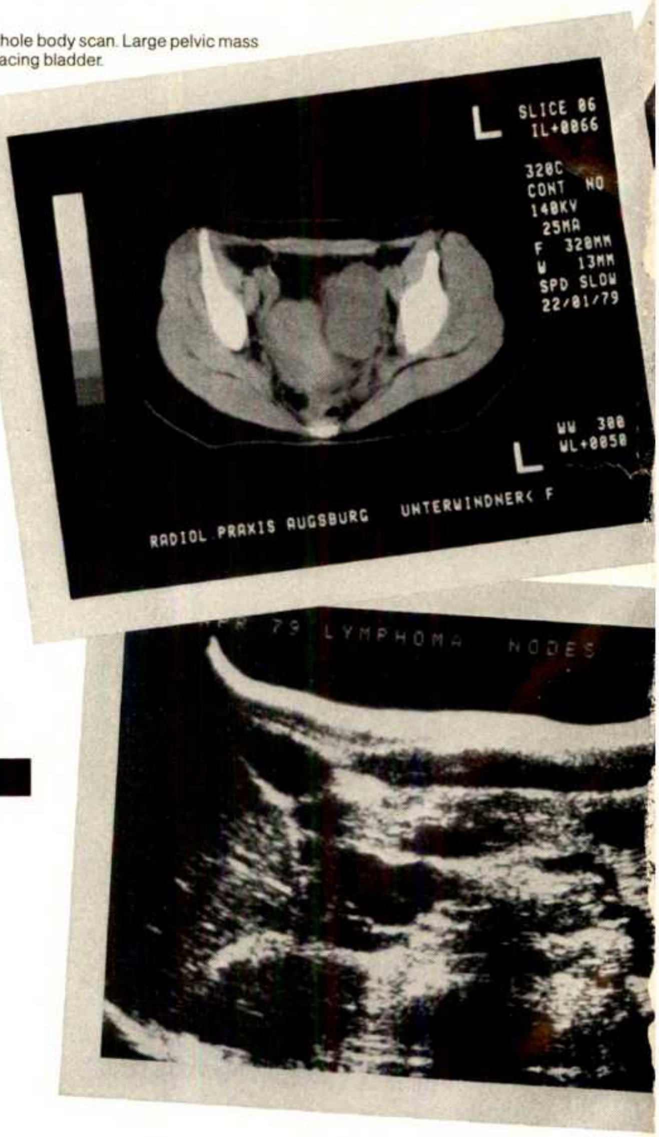
ADDRESS (block caps) ....

....

....

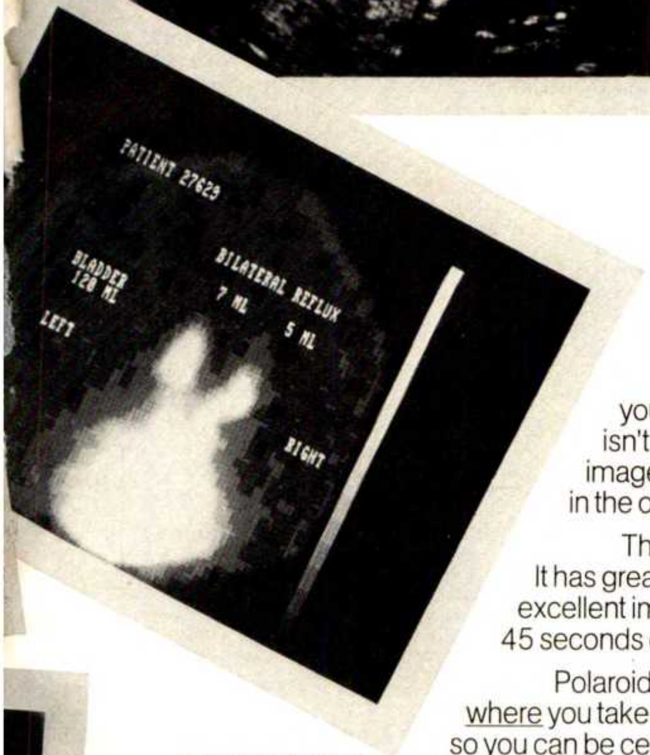
BJR0180

Introducing more greys to let you see more.



CT whole body scan. Large pelvic mass displacing bladder.

Hepatomegaly. Multiple confluent lesions in mid and posterior portion of right lobe of liver. Normal right kidney is also shown.



Radionuclide cystogram.

Lymphoma. Mass of nodes anterior to inferior vena cava, extending into the porta hepatis.

Polaroid has just added an instant film that reveals the diagnostic details better than ever. This new Type 611 is ideal for Grey Scale Recording in Ultrasound Tomography, Scan-converted Nuclear Medicine and Thermography.

The new film has an expanded dynamic range which makes it possible to record an extended grey scale. This in turn makes the film easy to use. You can set your video monitor for the best visual image and then photograph what you actually see. The contrast your eye sees as the best image is the contrast the film will record.

This expanded dynamic range also gives you greater exposure latitude. Even if the exposure isn't exactly right it will still give you a good diagnostic image. It also compensates for possible electronic drift in the output of the display.

The Type 611 is easier to use for still other reasons. It has greater overdevelopment stability. It will still yield an excellent image even if left for several minutes over the 45 seconds development time.

Polaroid instant photography gives you your results where you take the picture and while the patient is still in place, so you can be certain you have the information you need. Simplicity, convenience and immediate results – these make Polaroid films the recording medium of choice.

Polaroid offers you more than just films.

We have specialists who are available to help you with your diagnostic imaging. We will provide you with technical information on all of our instant films and training materials and we will help train your staff in their use.

For more information dial 100, ask for Freefone 2143 and speak to Ray Taylor or write to
Polaroid (U.K.) Ltd., Medical Products Sales,
Ashley Road, St. Albans, Herts AL1 5PR.
In the Republic of Ireland, contact:
Miniphoto Ltd., Darndale Industrial Estate,
Coolock, Dublin 5.

Polaroid

'Polaroid' is a registered trademark of Polaroid Corporation, Cambridge, Mass., USA. Copyright Polaroid Corporation 1979.

Ministry of Public Health – Kuwait

Diagnostic Radiologists

Applications are invited for Consultant and Senior Registrar Posts in Diagnostic Radiology in the Ministry's modern well equipped X-ray Departments. Air conditioned furnished accommodations are provided. Salaries decided according to qualifications and experience.

Short listed candidates will be interviewed in London.

Applications should be addressed to:
Dr. Na'il A. Al-Naqeeb, Under Secretary,
Ministry of Public Health, P.O. Box 5,
Kuwait, enclosing complete Curriculum Vitae.

Radiology in Killarney

with

The University of Connecticut

Killarney (Ireland) September 20–27, 1980

An international radiology symposium devoted to postgraduate radiology teaching. Emphasis will be placed on recent advances such as Ultrasound including Real Time, CT scanning, interventional and therapeutic radiology.

The distinguished international guest faculty includes **Drs. Erik Boijsen (Lund, Sweden), Peter Cooperberg (Vancouver), Robert Fraser (Alabama), Anthony Lalli (Cleveland), Glynn Lloyd (London), Maer Ozonoff (Newington Children's Hospital), William Park (Oswestry Orthopaedic Hospital), and Patrick F. Sheedy III (Mayo Clinic),** together with members of the Faculty of Radiologists in Ireland who will augment the University of Connecticut faculty.

For further details, contact the Program Director:

D. Beatty Crawford, M.D.
Department of Radiology
University of Connecticut Health Center
Farmington, Connecticut 06032 U.S.A.

The British Journal of Radiology
REPRINTS

	Price	BIR Members Price
Proceedings of the Symposium on the Effects of Low Radiation Doses on the Maturation of the Developing (human) Ovum and Foetus	60p	40p
Fourth Progress Report on the B.I.R. Fractionation Study on 3F/week or 5F/week Treatment of Larynx and Pharynx	30p	30p
Fifth Progress Report on the B.I.R. Fractionation Study on 3F/week or 5F/week Treatment of Larynx and Pharynx	50p	50p
Sixth Interim Progress Report of the B.I.R. Fractionation Study of 3F/week versus 5F/week in Radiotherapy of the Laryngo-pharynx (April 1978)	60p	60p
Neurology's Debt to Becquerel (Mackenzie Davidson Memorial Lecture) by J. W. D. Bull	30p	30p
The Support of Scientific Research (Silvanus Thompson Memorial Lecture) by Professor Sir Brian Flowers	60p	60p
Memorandum on Implementation of the Second Report of the Adrian Committee on Radiological Hazards to Patients	*FREE	FREE
New methods of imaging in diagnostic radiology (Silvanus Thompson Memorial Lecture) by H. E. Johns (September 1976)	75p	75p
Hyperbaric oxygen and radiotherapy: a Medical Research Council trial (1978)	†FREE	FREE

*If you are only ordering this reprint please enclose a stamped addressed foolscap envelope.

†Applications to the Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG with a stamped addressed envelope.

Available from the Publications Office, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (remittance with orders less than £2, please)

E-Z-PAQUE

Barium sulphate for suspension

For routine studies of the Upper G.I. Tract.

Rapid Transit E-Z Paque T.M.
Barium Sulfate for Suspension
FRESH FRUIT FLAVOR
NET WT. 177 GM. (6.2 oz.)
PAT. #3773243
G.I. Cup
E-Z-EM
E-Z-Jug
WITH FRESH FRUIT FLAVORED E-Z-PAQUE®
(Barium Sulfate for Suspension)
CONTENTS
INSTRUCTIONS
LOT NO.
Special formulation for upper gastrointestinal examination of the esophagus, stomach and small bowel.
E-Z-EM CO. INC. 7 PORTLAND AVENUE, WESTBURY, N.Y. 11590

Low cost. Available in single dose cups or handy E-Z-JUGS.
Each jug yields 1200 mls at 100%w/v.

Further details available from sole U.K. distributors:

Henleys Medical Supplies Ltd.
London N8 ODL 01-889 3151

E-Z-EM ®

PL/1665/0002

FARMER
DOSEMETER
2570

A New Generation Microprocessor System

Improved accuracy, precision and simplicity of operation are major features in this new generation microprocessor dosemeter. Facilities include: a fully auto-corrected readout with keyboard entry of pressure, temperature and chamber correction factors; and keyboard entry of time for measurement of dose and exposure.

Operator's error is minimised by arrangement of controls, and the information display indicates mode of operation, corrections applied, dose range multiplier and unit of measurement.

The fully portable and battery operated 2570 is offered with a 0.6cm³ chamber which is conveniently housed in the instrument case. In-built facilities are provided for conversion to readout in unit absorbed dose, gray.

Full details on request.

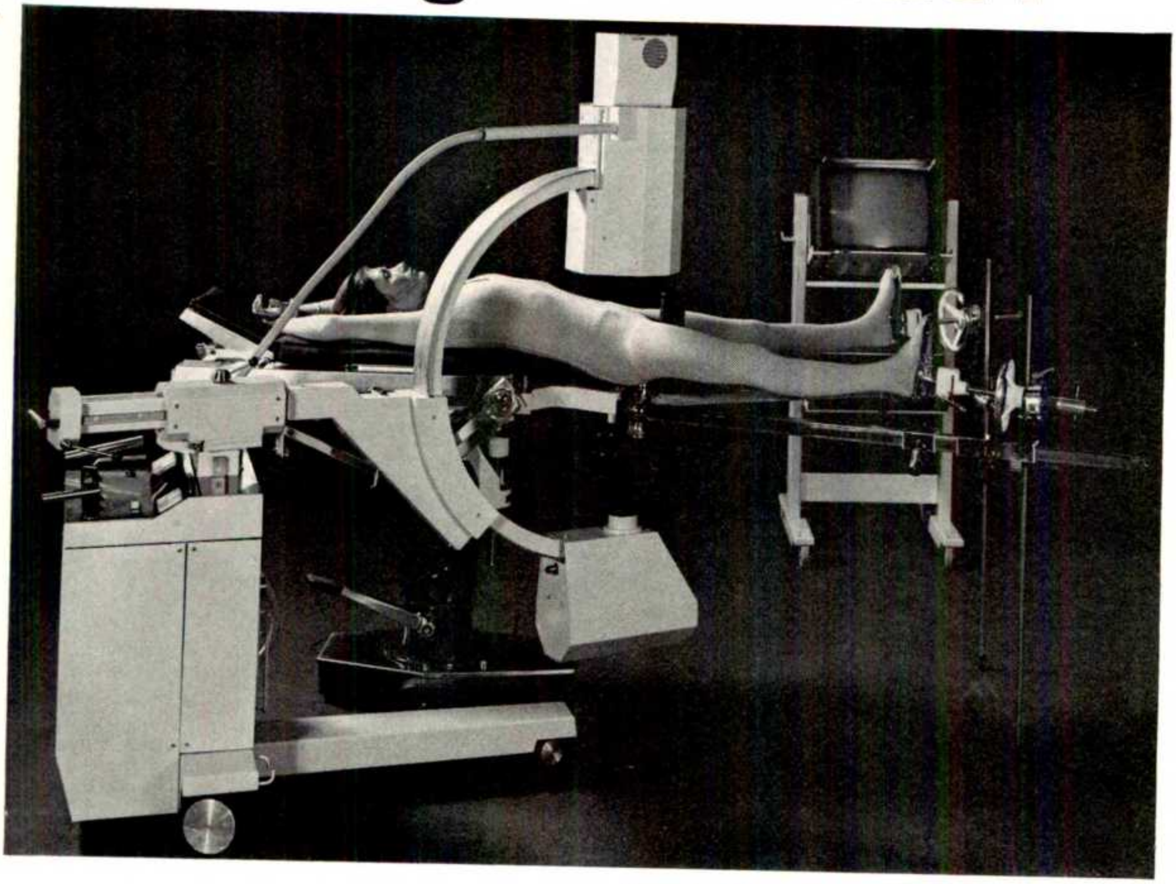
SAFETY FEATURES

- **Keyboard disabled during measurement.**
- **Measurement aborted if switches are operated during measurement.**
- **Built-in display clock.**
- **Indication of "off zero" condition and adjustment required clearly shown on information Display.**
- **Measurement of applied dose, if any, continues even after Trip Output is actuated.**
- **Elimination of range setting errors.**
- **Unit of measurement and associated multiplier displayed automatically.**

NUCLEAR ENTERPRISES LIMITED

Bath Road, Beenham, Reading, RG7 5PR, England.
Tel: 073-521 2121. Telex: 848475.
Cable: Devisotope, Reading.
Also at: N.E. Nuclear Enterprises, Geneva.
Nuclear Enterprises GmbH, Munich.
Nuclear Enterprises, San Carlos, U.S.A.

A rapid and precise surgical X-ray system with high-resolution TV



The streamline design for the CGR Optascop increases the range of applications in surgical radiology. Easier manipulation and greater mobility by steering castors allow precise positioning from the simplified control panel.

A complete mobile high-definition intensifier unit equipped with a TV camera and separate trolley-mounted monitor.

The dual focus x-ray tube with remote controlled collimator provides for radiography and fluoroscopy up to 100kV. The x-ray tube – intensifier TV movements are motor driven.

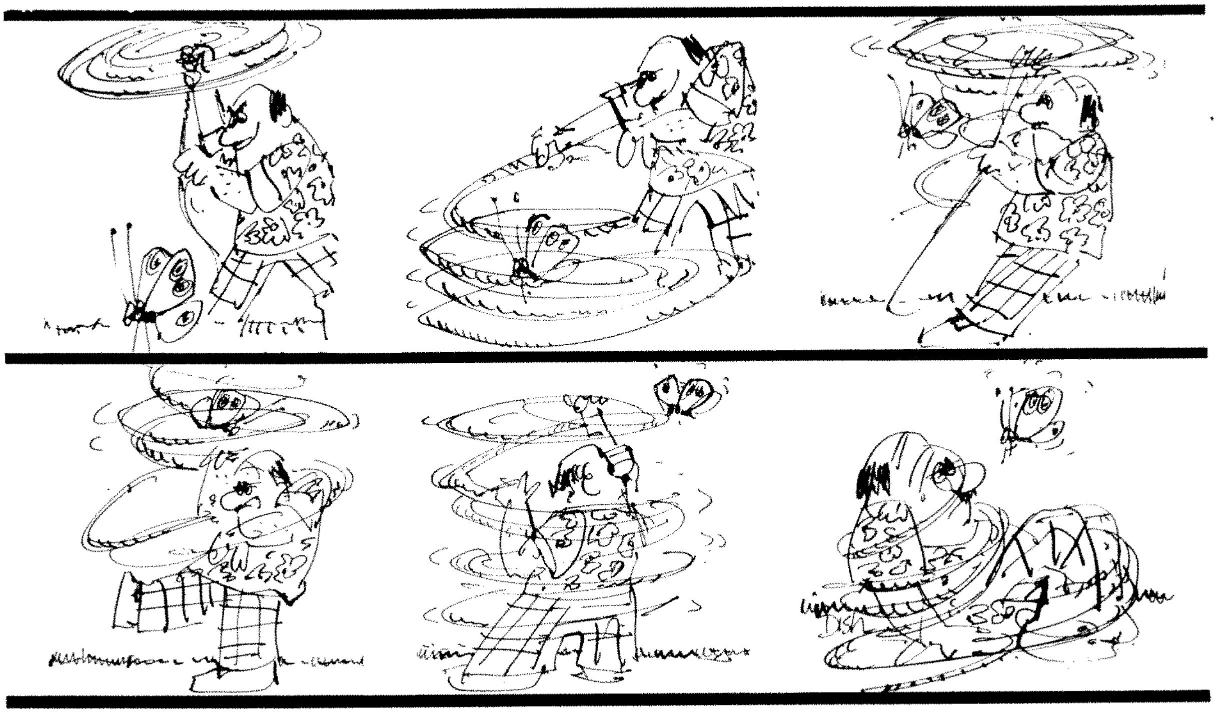
Optional extras are dose reduction pulsed fluoroscopy, and taped memory facility.

OPTASCOP

from

CGR

Full details and specification from
CGR MEDICAL LIMITED
Astronaut House, Feltham, Middx. Tel: 01-890 8166



Have you ever tried catching butterflies with a lasso?

In fact it's about as difficult as trying to record grey scale detail on high contrast film.
Until now only high contrast films have been available for recording Nuclear Medicine, C.T. Scan and Ultrasound images even though the latter does contain subtle grey scale detail.
At ILFORD we realized just how difficult this situation could be and so, being experts in image recording, we did something about it.
The results of our research are two new films each designed for its own specific purpose.
ILFOSCAN (SP422X) a relatively high contrast film for Nuclear Medicine and C.T. Scanning applications and ILFOSOUND (SP440X) for recording the grey scale detail of Ultrasound.
These two films are the sensible solution to a serious problem. In short, two nets where a lasso wont do.
After all, who enjoys being tangled up in their work.

ILFOSOUND (SP440X) The right film for Ultrasound.
ILFOSCAN (SP422X) The film for Nuclear Medicine and CT Scanners.

ILFORD
ILFORD Limited · Basildon · Essex SS14 3ET

THE GENERAL HOSPITAL

Diagnostic Radiologist is required with experience and interest in

NEURORADIOLOGY

including C.T. scanning department in process of negotiating installation of C.T. scan. Recently opened modern diagnostic department with large and interesting workload in tertiary care university hospital. Opportunities exist for teaching and for clinical and basic science research.

Please apply to:
Chairman
Department of Radiology
The General Hospital
Health Sciences Centre
Prince Philip Drive
St. John's
Newfoundland
Canada A1B 3V6

THE GENERAL HOSPITAL

Diagnostic Radiologist required with interest and experience in

GENERAL and VASCULAR RADIOLOGY and ULTRASONICS

for recently opened modern diagnostic department with large and interesting workload in tertiary care university hospital. Opportunities exist for teaching and for clinical and basic science research.

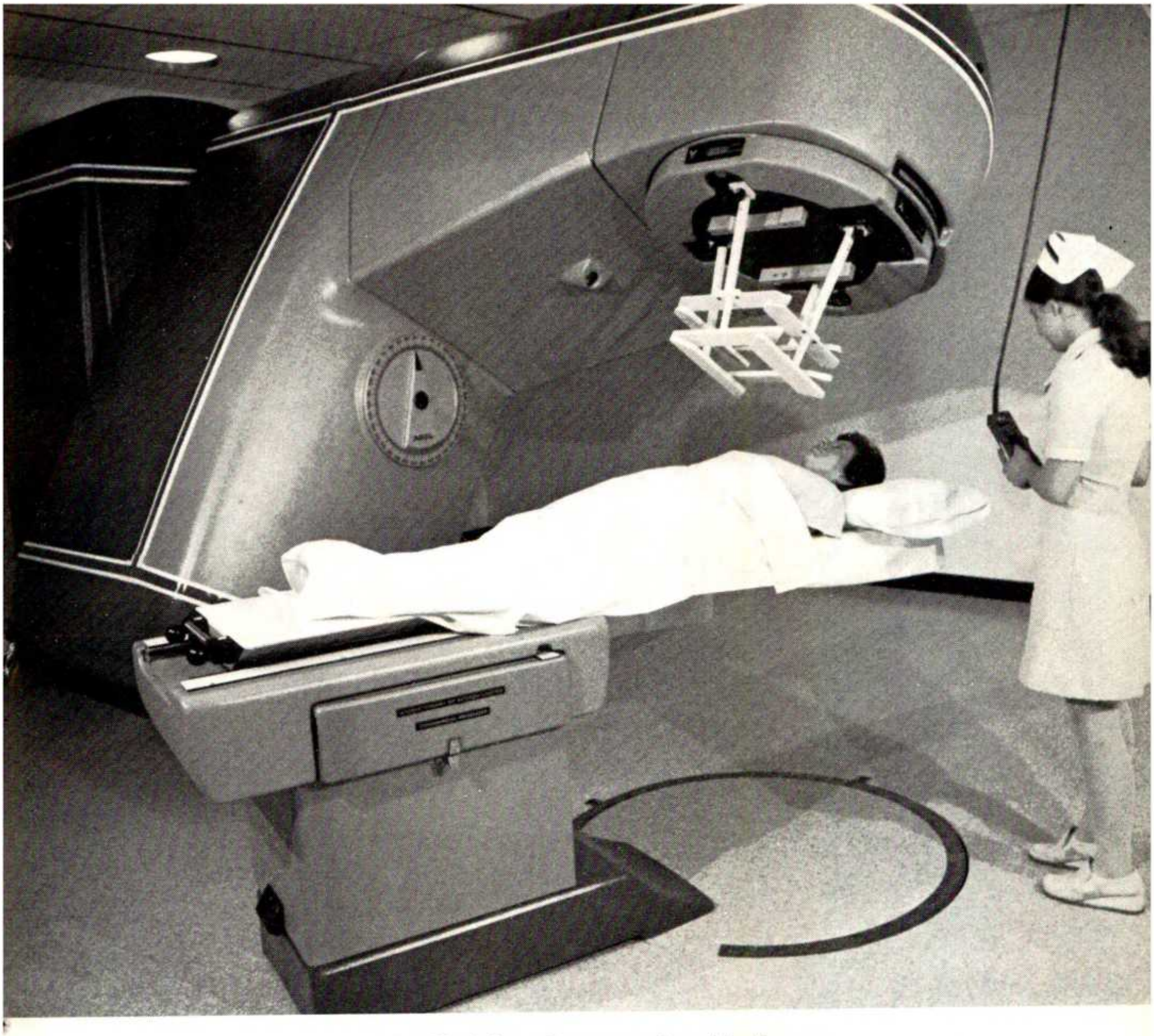
Please apply to:
Chairman
Department of Radiology
The General Hospital
Health Sciences Centre
Prince Philip Drive
St. John's
Newfoundland
Canada A1B 3V6

The London Ultrasound Course for Radiologists

April 21st–25th 1980

This new course in clinical ultrasound is designed to cover non obstetric abdominal scanning in depth, but will also include certain other applications. The course will be held in a London hotel and will be limited to 50 participants.

Course leaders:–
David Cosgrove   Keith Dewbury   Hylton Meire
Further information from:–
Dr. H. B. Meire, Clinical Research Centre, Harrow, Middlesex
HA1 3UJ U.K.



Reliable. Accurate. Unique.

Therac 6 and Therac 20 Linear Accelerators from AECL.

Atomic Energy of Canada Limited presents two ruggedly built, precision engineered linear accelerators which have been designed and proven to deliver years of dependable service — Therac 6 (6 MV photons) and Therac 20 (18 MV photons and 6-20 MeV electrons).

Each possesses a number of unique advantages including large fields in both photon and electron modes, with no primary collimator cut-off. Specific to the Therac 20 is its beam scanning and trimmer bar system which accurately defines infinitely variable electron field sizes up to the largest currently available. Another singular aspect of Therac 20 is the option of dual photon beams which along with the standard electron beams offer exceptional treatment flexibility.

Low isocentric height and high isocentric accuracy are common to both the 6 and 20 as is the 360° collimator rotation with wedged or blocked fields for simplified set-up. Our new, fully motorized accelerator couch features free float on lateral and longitudinal motions. Advanced computer controls with record and verify, superior dose uniformity and depth dose characteristics, and a high, constant output all contribute to maximizing patient throughput.

Your complete satisfaction is assured beginning with our initial sales contact and continuing through architectural planning, installation supervision, final acceptance, and our world-wide 24 hour service support. For full information on Therac 6 and 20, contact AECL — where radiotherapy has been our business for over a quarter of a century.

Atomic Energy
of Canada Limited
Medical Products

P.O. Box 6300, Ottawa, Canada K2A 3W3 Tel.: (613) 592-2790. Cable Nemota. Telex: 053-4162.
In the United States: Chicago: (312) 593-3242. Philadelphia: (215) 441-5353. Atlanta: (404) 987-9280. Dallas: (214) 233-0939. Los Angeles: (714) 989-3900.
In Australia: P.O. Box 57 Crow's Nest North, Sydney 2065 NSW. And agents throughout the world.

ENSIGN a new table
built for patient and operator ease

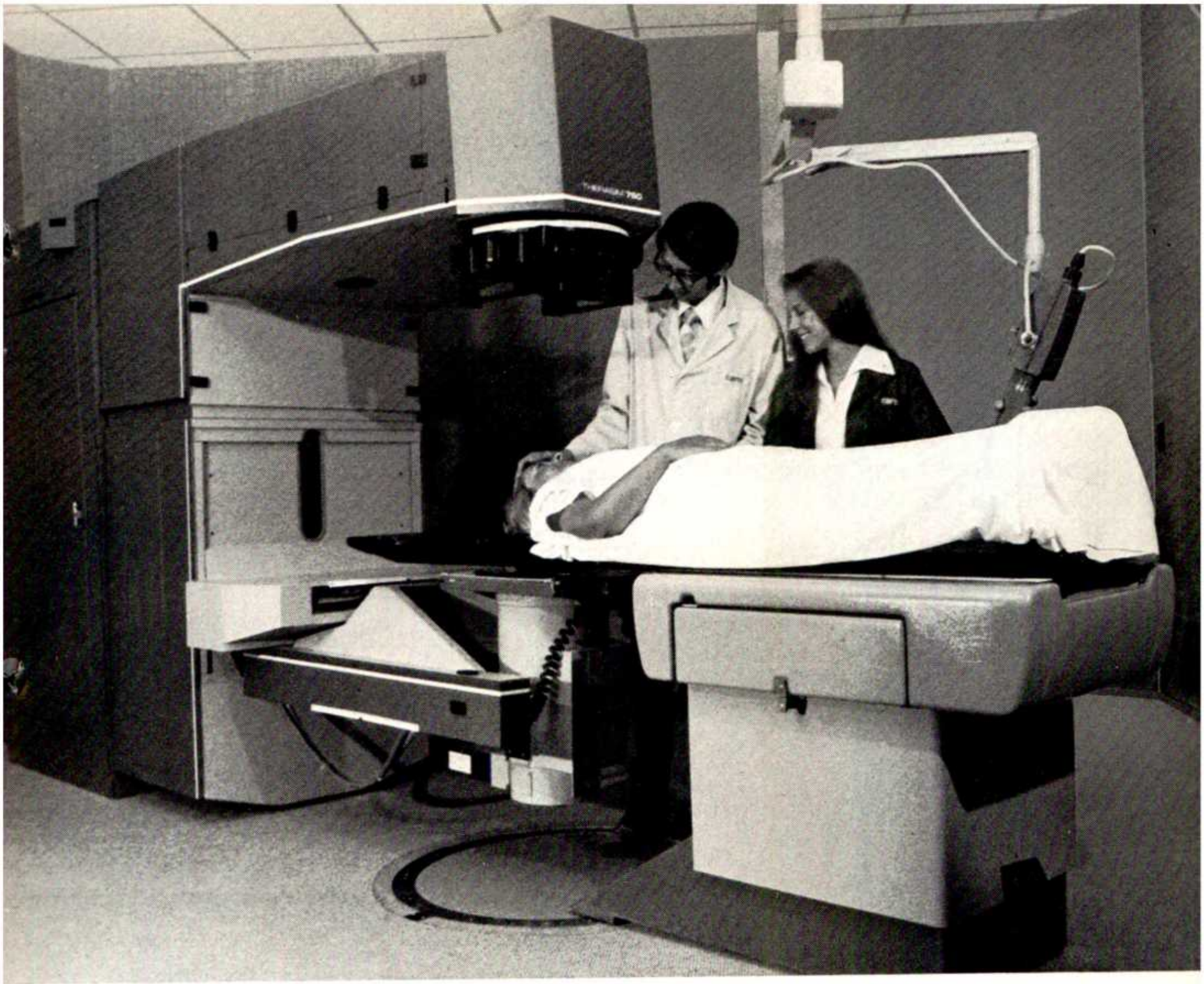
A superb floating top table
with exceptional operator
convenience and flexibility

IN ORDINARY TERMS a motorised variable height Bucky table that easily adjusts from a height of 81 cms (32 ins) to as low as 50 cms (19½ ins).

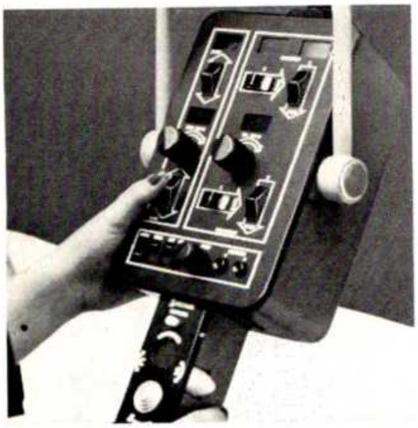
IN CLINICAL FACT a design full of human engineering to help the injured and infirm. A design where patient comfort and safety are essential factors within the specification.

GEC
Medical

GEC MEDICAL EQUIPMENT LIMITED
P.O. Box 2 · East Lane · Wembley · Middlesex · HA9 7PR · England
Telephone: 01-904 1288 · Telex: 922177 · Cables: Skiagram Wembley



Rugged, Precise, Adaptable
Therasim 750 Universal Simulator from AECL



Therasim 750 Universal Simulator from Atomic Energy of Canada Limited produces the widest possible range of simulation characteristics with rotational radiotherapy units of all type and manufacture. It is particularly compatible with AECL's Theratron 780 and 80 Cobalt units and Therac linear accelerators. In addition, Therasim has been designed to work in concert with computer controlled treatment planning systems such as the AECL TP-11.

With exceptionally rugged frame and carriage construction, Therasim will accommodate the heaviest, high output components while ensuring the ultimate in isocentric accuracy. The image intensifier's extensive travel capability provides the necessary flexibility to cover all conceivable treatment situations and a longer, variable S.A.D. simplifies machine set-up. Therasim 750 permits accurate coverage of large treatment fields in excess of 45cm X 45cm while standard 35.6cm X 43.2cm cassettes are used for storing data. A fully motorized, five motion couch is isocentrically mounted with extra structural rigidity for optimum accuracy of patient set-up. A special stretcher top constructed of carbon fibre is extremely stiff with minimum beam attenuation. Convenient and simple to operate, all Therasim machine functions can be precisely directed from either the local (hand) control within the treatment room or from the console. Both locations feature easy to read, continuous digital displays and backlit panels.

With a quarter of a century devoted to the design and manufacture of advanced radiotherapy equipment, AECL extends the tradition with the Therasim 750 Universal Simulator. For complete information, contact us.

Atomic Energy
of Canada Limited
Medical Products

P.O. Box 6300, Ottawa, Canada K2A 3W3, Tel.: (613) 592-2790. Cable Nemota. Telex: 053-4162.
In the United States: Chicago: (312) 593-3242. Philadelphia: (215) 441-5353. Atlanta: (404) 987-9280. Dallas: (214) 233-0939. Los Angeles: (714) 989-3900.
In Australia: P.O. Box 57 Crow's Nest North, Sydney 2065 NSW. And agents throughout the world.

As a radiology teacher, it's unbeatable

(The Temex Phantom from James Girdler)

When you want to learn or demonstrate the effect of a radiotherapy technique within the human body, there is no better teacher than a natural skeleton embodied in rubber casting material designed to absorb and scatter radiation in the same ways as human tissue.

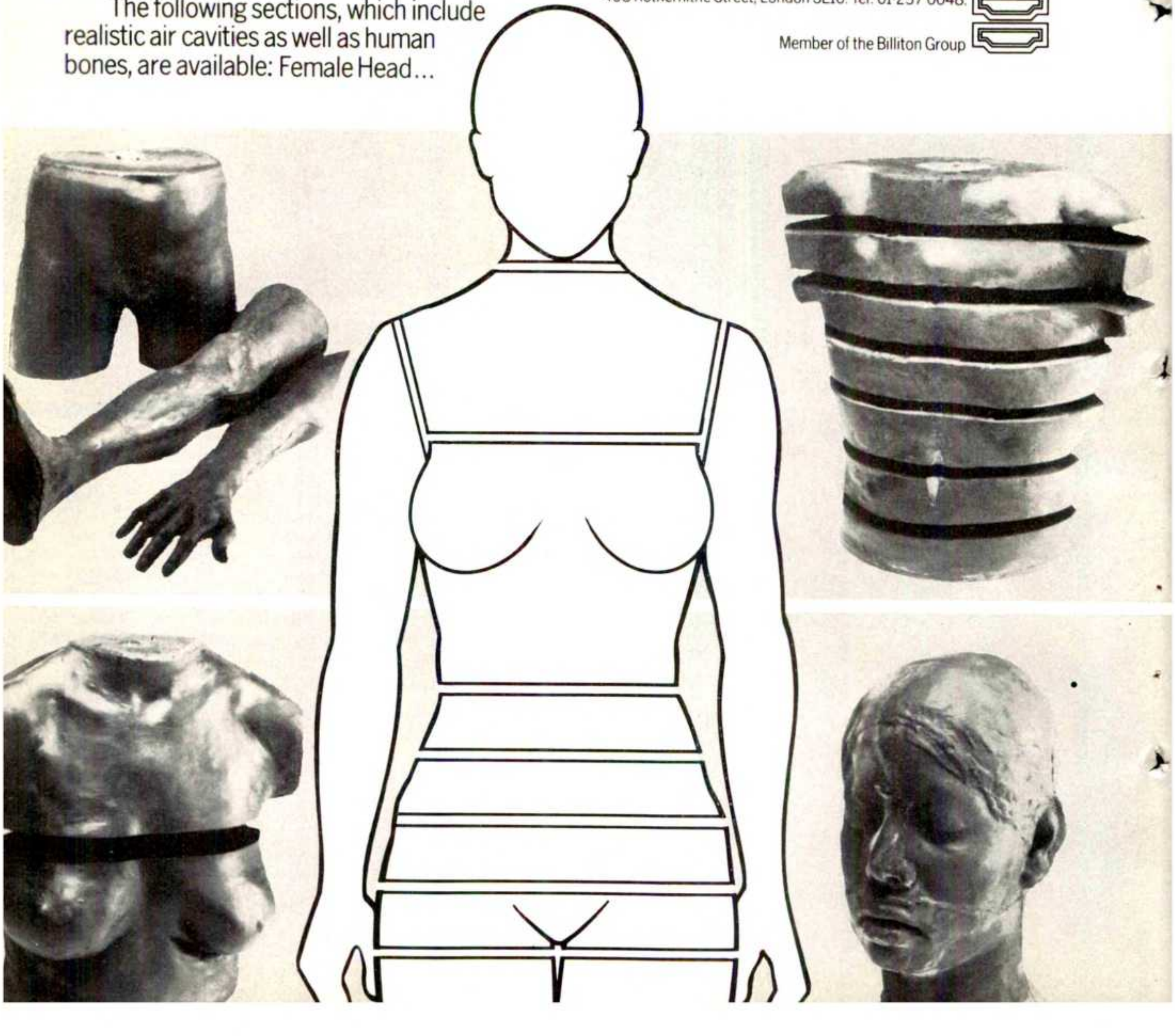
Temex Phantoms are also of great value in diagnostic radiology both in setting up X-ray equipment and in estimating optimum exposure conditions.

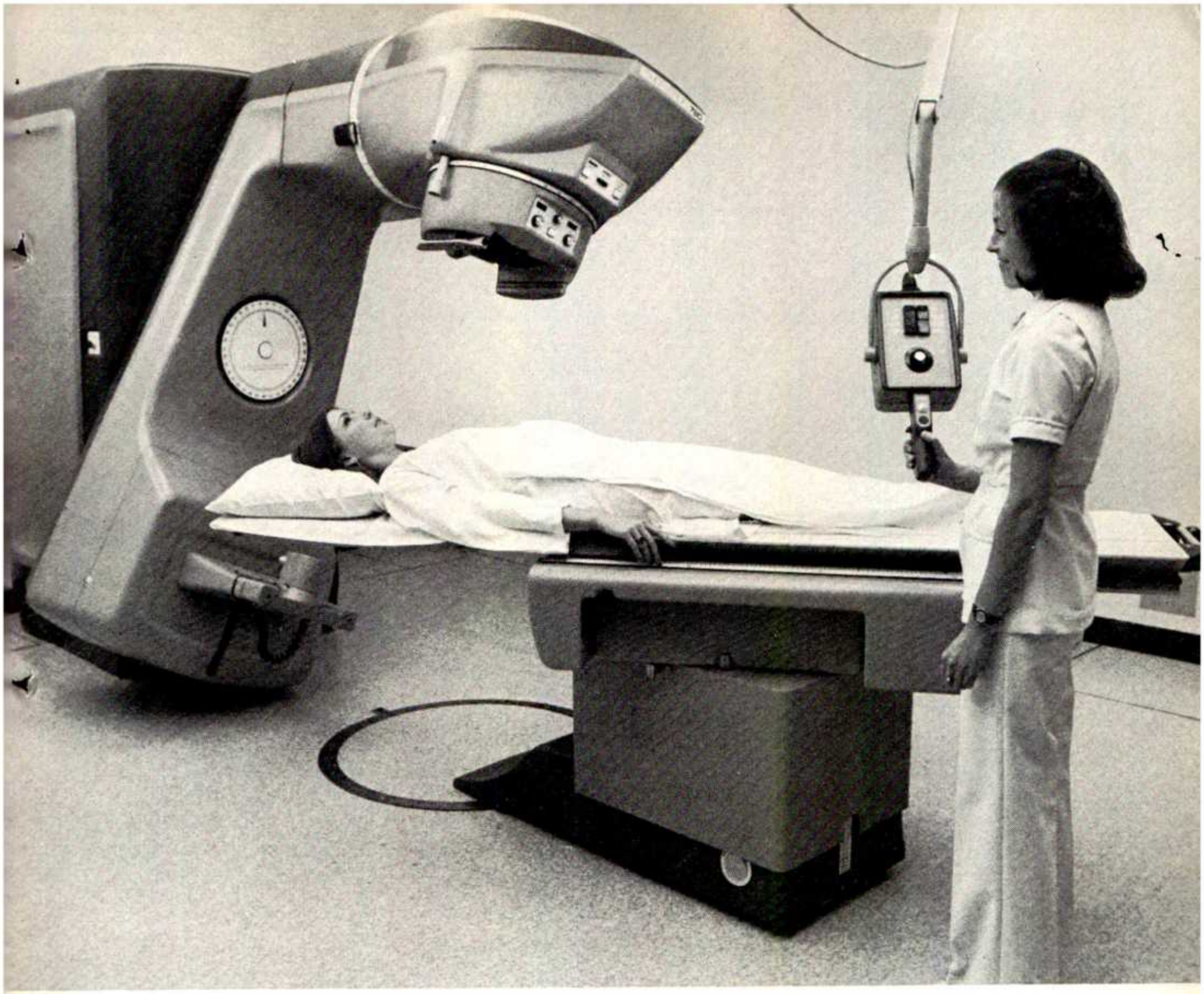
The following sections, which include realistic air cavities as well as human bones, are available: Female Head... Male Head... Female Thorax... Male Thorax... Lungs... Female Pelvis... Female Trunk... Female Right Hand... Female Right Hand and Forearm... Female Right Leg... Dental Phantom.

Please contact us for more information on Temex Phantoms or the full James Girdler range of lead shielding, components and protective products for hospitals.

James Girdler & Co Ltd
458 Rotherhithe Street, London SE16. Tel: 01-237 0048.

Member of the Billiton Group





Dependable. Versatile. Economical.
Theratron 780 Cobalt 60 Unit from AECL.

The Theratron 780 Cobalt 60 unit is a powerful combination of dependability and versatility from Atomic Energy of Canada Limited. Sturdily constructed, it has low maintenance and shielding requirements, and represents a highly reliable, trouble-free concept of teletherapy treatment at low capital cost. The reliability of AECL cobalt therapy equipment is best exemplified by the fact that 8 of our original units, built over 25 years ago, still remain in service.

The versatile Theratron 780 allows you to match the source (and cost) to your specific clinical needs, all the way up to 200 rmm. For example, a small clinic with a light patient load could use a correspondingly small source. Primarily known for its effectiveness at superficial and medium depths, Theratron 780 is capable of effective treatment at all depths. Since its beam is essentially monochromatic, resulting in minimal skin reaction, it is frequently the number one choice for head and breast treatments. A fully motorized couch with free float on lateral and longitudinal motions enables quick set-up, optimizing patient throughput. In addition, a large variety of optional accessories are available to suit your specific treatment procedures.

AECL is your comprehensive centre for all your teletherapy treatment needs. Every aspect is efficiently covered from our initial sales contact through architectural planning, installation supervision, final acceptance, to our world-wide, 24 hour, service support. What's more, we manufacture and load the sources. In fact, over 3000 AECL beam therapy sources have been supplied to the international marketplace. For full information on Theratron 780 or any other product, contact AECL — where radiotherapy has been our business for over a quarter of a century.

Atomic Energy of Canada Limited
Medical Products

P.O. Box 6300, Ottawa, Canada K2A 3W3. Tel.: (613) 592-2790. Cable Nemota. Telex: 053-4162.
In the United States: Chicago: (312) 593-3242. Philadelphia: (215) 441-5353. Atlanta: (404) 987-9280. Dallas: (214) 233-0939. Los Angeles: (714) 989-390

PRM 80

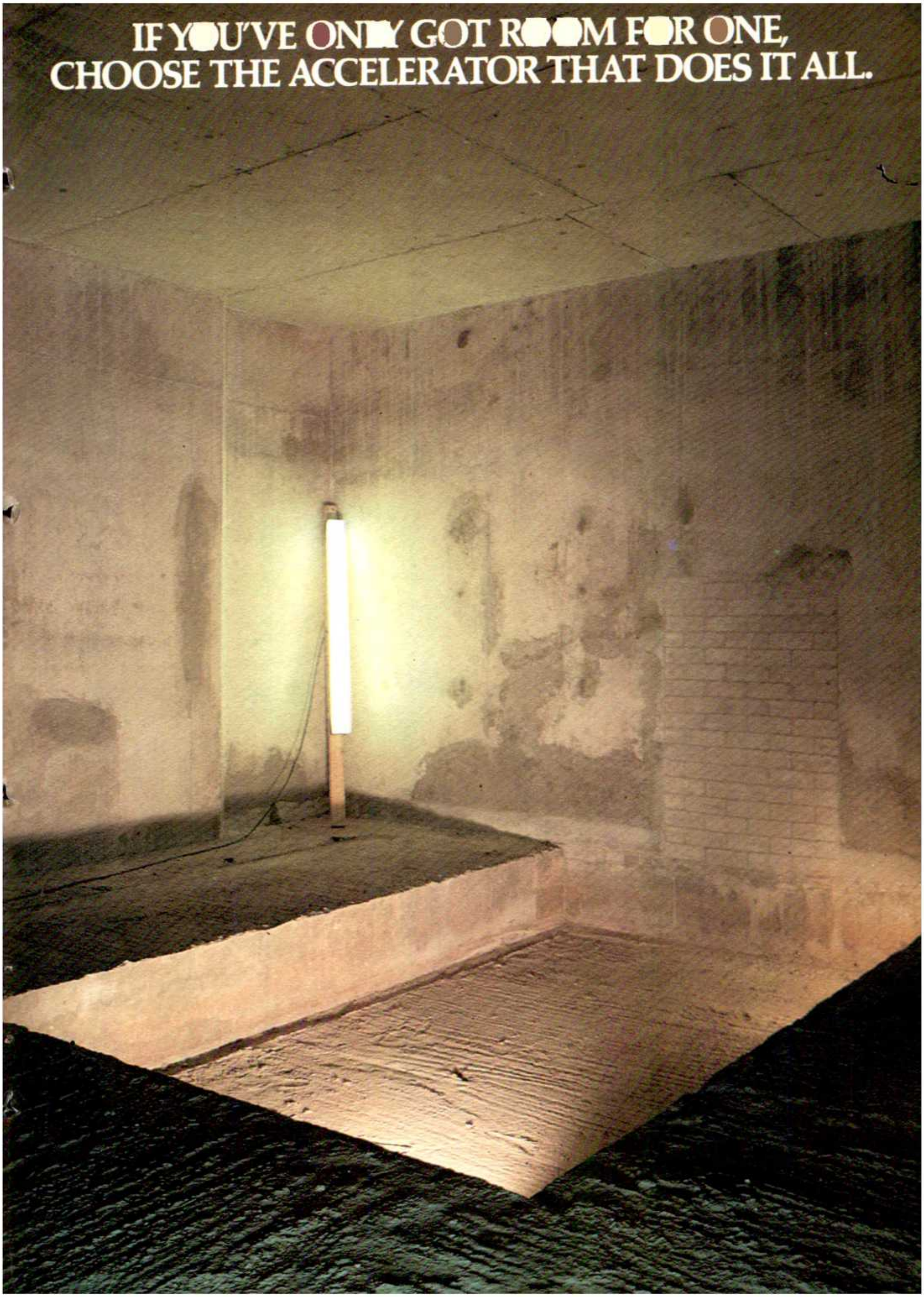
The T.E.M. programmed radiotherapy microcomputer has been developed to handle the everyday task of accurately calculating a patient's treatment dose and/or time.

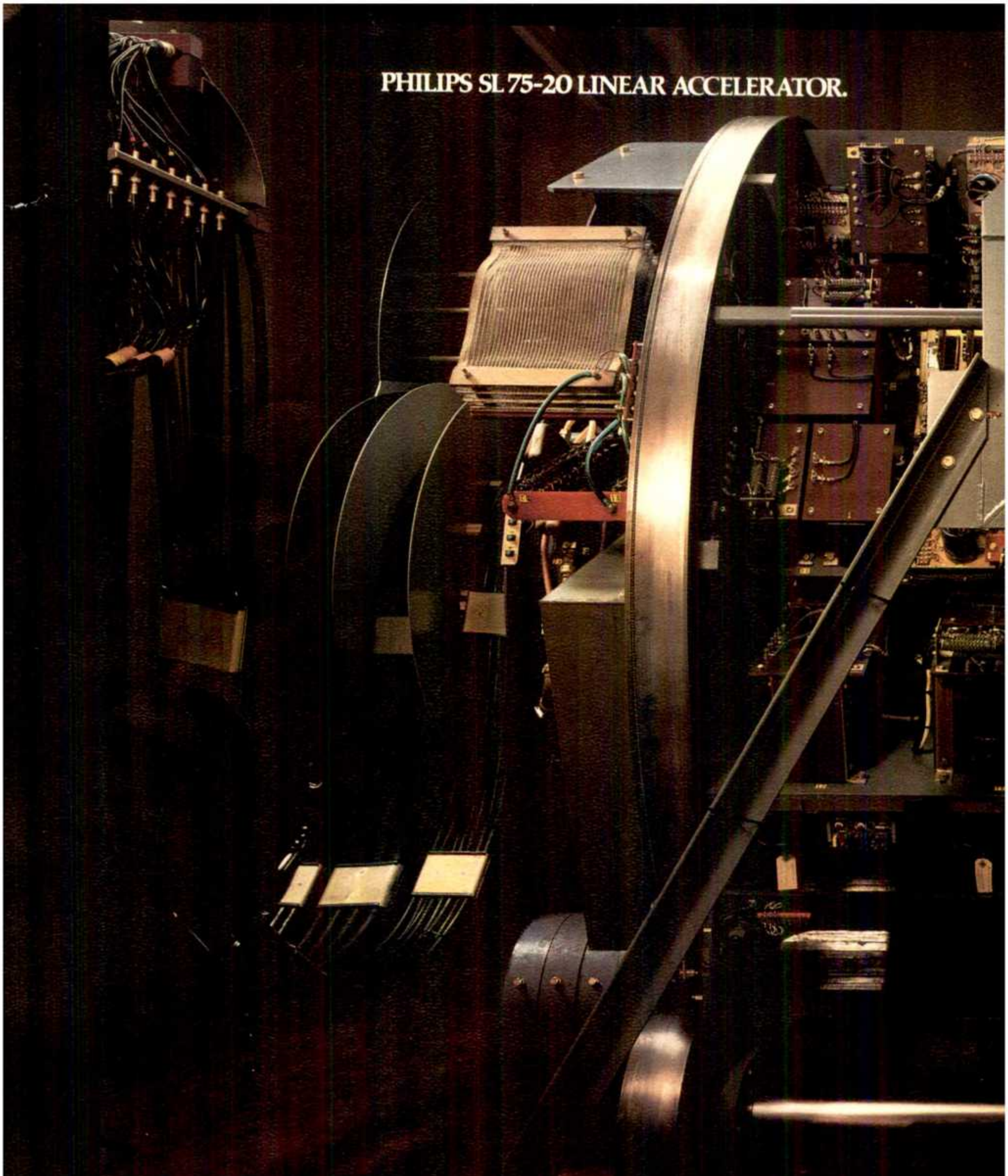
From these entries:	The PRM 80 gives:
Field sizes	Treatment Time
S.S.D.	Set Dose
Attentuation Factors	Skin Dose.
Depth of Tumour	
Prescribed Dose Etc.	

Capable of calculating opposed field and off-axis data, the PRM 80 also has an optional facility giving the total number of treatments, cumulative dose and the ret dose.

The PRM 80 prints out all this data, including the actual treatment time which is recorded from its own internal timer.

TEM **TEM Instruments Limited**
Gatwick Road, Crawley, Sussex, RH10 2RG, England
Tel: 0293 31244 Telex: 87397, Grams: TESTMENT CRAWLEY


IF YOU'VE ONLY GOT ROOM FOR ONE,
CHOOSE THE ACCELERATOR THAT DOES IT ALL.



PHILIPS SL 75-20 LINEAR ACCELERATOR.

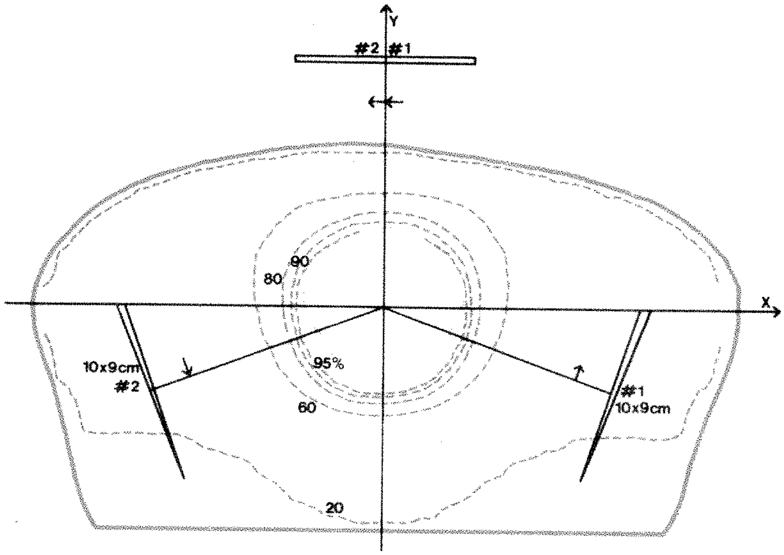
BACKED BY OVER 30 YEARS EXPERIENCE IN ACCELERATOR DESIGN.

- Demountable electron gun eliminates the need to replace an entire waveguide structure every two to three years.
- Servo beam control systems maintain uniform field flatness and stable depth dose characteristics under all treatment conditions.
- Long term mechanical accuracy is assured through low wear rates on the rotating drum structure.
- Easy access to all control equipment and gantry components for simplified servicing.
- Hermetically sealed ionisation chamber eliminates the need for constant recalibration to compensate for changes in barometric pressure and temperature.

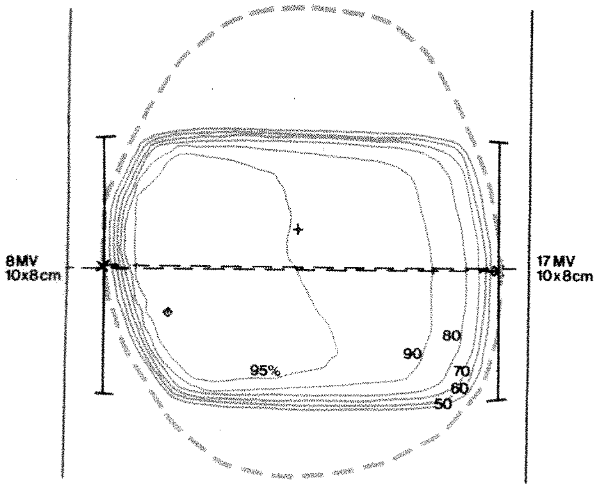
A COMPLETE RADIATION THERAPY DEPARTMENT IN ONE ACCELERATOR.

- * Two X-ray energies at 8 and 16MV meet the clinical requirements for intermediate and deep treatments.
- * Eight electron energies from 5 to 20MeV and a wide range of electron applicators give unrivalled versatility for electron therapy.
- * Combined 8MV and 16MV X-ray treatments or combined X-ray and electron treatments
- * Highly versatile patient support systen facilitate all types of treatment technic
- * Maximum X-ray field size of 40 x 40cn the isocentre enables mantle fields of n than 60 x 60cm to be delivered at exter source – skin distances.
- * The addition of a Vericord system enha treatment accuracy and simplifies recc keeping

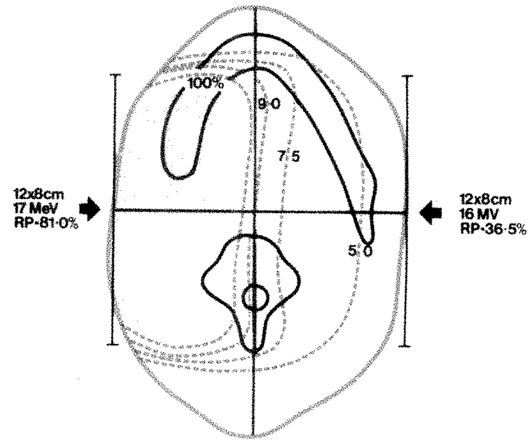
RESULTS THAT SPEAK FOR THEMSELVES.



SL75 – 20. Addenbrookes Hospital, Cambridge, England.
8 MV Wedge Rotational Isocentric X-ray treatment.



Combined 17 MV and 8 MV X-ray treatment.
SL75 – 20. University of Florida, Gainesville, Florida, USA.



Combined 16 MV X-ray and 17 MeV electrons treatment.
SL75 – 20. University of Gothenberg, Gothenberg, Sweden.

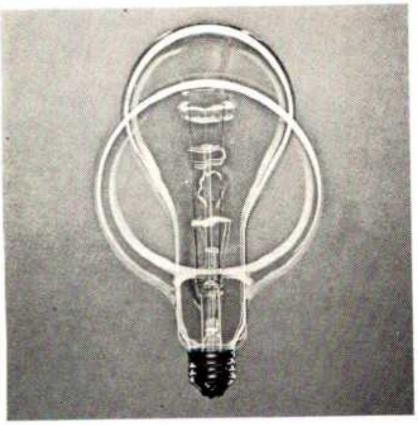
Contact Philips at one of the addresses shown below
for more information on our full range of equipment for radiation therapy.

Philips Medical Systems, Kelvin House, 63/67 Glenthorne Road, Hammersmith, London W6 0LJ.
M.E.L. Manor Royal, Crawley, Sussex RH10 2PZ.
Divisions of Philips Electronic & Associated Industries Ltd.
Philips Medical Systems Inc, 710 Bridgeport Avenue, Shelton, Connecticut 06484, United States of America.
N.V. Philips, Medical Systems Division, Eindhoven, The Netherlands.

Centre photographs by courtesy of Clatterbridge Hospital West, Bebington, Wirral, Cheshire, U.K., and Cookridge Hospital, Leeds, U.K.

PHILIPS Together we can build for the future today PHILIPS Medical Systems

Simultaneous treatment planning and information management.
TP-11 and TRIM from AECL.



Atomic Energy of Canada Limited has taken two ideas and made them work better as one. The resulting combination allows, for the first time, simultaneous treatment planning and information management.

Half the combination is TP-11, an interactive, computerized, radiotherapy planning system which eliminates the need for tedious and often imprecise manual planning. It is capable of a wide variety of plan calculations utilizing a virtually unlimited number of beams. Dose distributions are rapidly calculated for fixed and moving rectangular photon and electron beams, irregular photon beams, and brachytherapy plans, using both point and linear sources. All plan types may be combined without practical limit. In addition, rapid modifications may be easily made, enabling the operator to select the optimum plan from a visual display. A hard copy plot can be produced and the plan is automatically stored. Included in the system is high quality PDP-11 computer hardware and a 50.8cm x 50.8cm sonic digitizer with sparking stylus for entry of graphic data.

TRIM, the Tumour Registry and Information Management system, forms the other half of the combination. Of particular benefit to the radiologist and epidemiologist, it represents a unique, interactive, multi-user approach to clinica data management. A complete and self-contained software system, TRIM car be used to enter, update, delete, and selectively retrieve patient data according to the specific needs as described by its user. Additional features include a readily expandable data base which can be customized to suit the user's requirements and software programs which allow transfer of data to a central data base.

Although both TP-11 and TRIM can operate independently of each other and in conjunction with other systems, they reach their maximum potential when usec together and with AECL's broad range of radiotherapy equipment. For full information on how TP-11 and TRIM can bring added dimensions of accuracy to your treatment planning and record keeping, contact AECL.

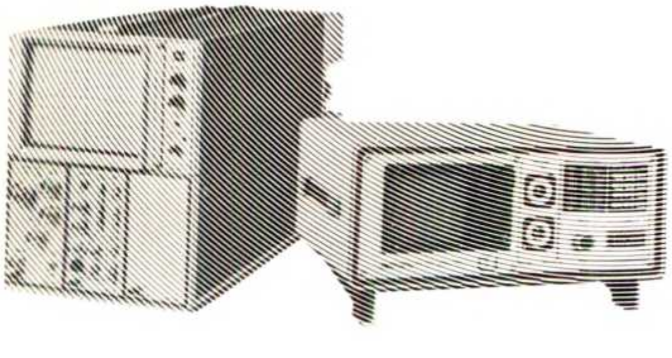
Atomic Energy of Canada Limited
Medical Products

P.O. Box 6300, Ottawa, Canada K2A 3W3. Tel.: (613) 592-2790. Cable Nemota. Telex: 053-4162.
In the United States: Chicago: (312) 593-3242. Philadelphia: (215) 441-5353. Atlanta: (404) 987-9280. Dallas: (214) 233-0939. Los Angeles: (714) 989-390
In Australia: P.O. Box 57 Crow's Nest North, Sydney 2065 NSW. And agents throughout the world.

40 years of experience and expert knowledge can be made yours very easily

Oldelft

Oldelft England Ltd
16 Barclay Road, Croydon CRO 1JN
Tel. (01) 681 1171, telex 946154



The complete range of ultrasound equipment: gray-scale scanners, motorized arc scanners, linear phased array real time scanners, sector phased array real time scanners, M-mode monitors and all accessories for recording data on line-scans or video systems.
This Toshiba ultrasound equipment is characterized by unrivalled image definition, simplicity of operation and professional design.
It is sold and serviced by Oldelft throughout Europe.

Radiodiagnosis
Odelca x-ray cameras
100mm System for spotfilm photography
Deltorax chest film changer
Odelscope image intensifier for fluoroscopy

Ultrasound
Real time linear phased array systems
Cardiac phased array sector scanners
General purpose gray-scale compound scanners

Nuclear medicine
Gamma cameras with complete range of accessories (e.g. multi-imager, whole body scanning bed)

Radiotherapy
4 and 15 MeV linear accelerators
Cobalt units

Radiotherapy planning
Simulix-Y simulator with Simtomix accessory for analog whole body tomography

Pulmonary function testing
Computerized equipment for the pulmonary lab
Automated procedures in spirometry, flow/volume loop analysis and exercise testing

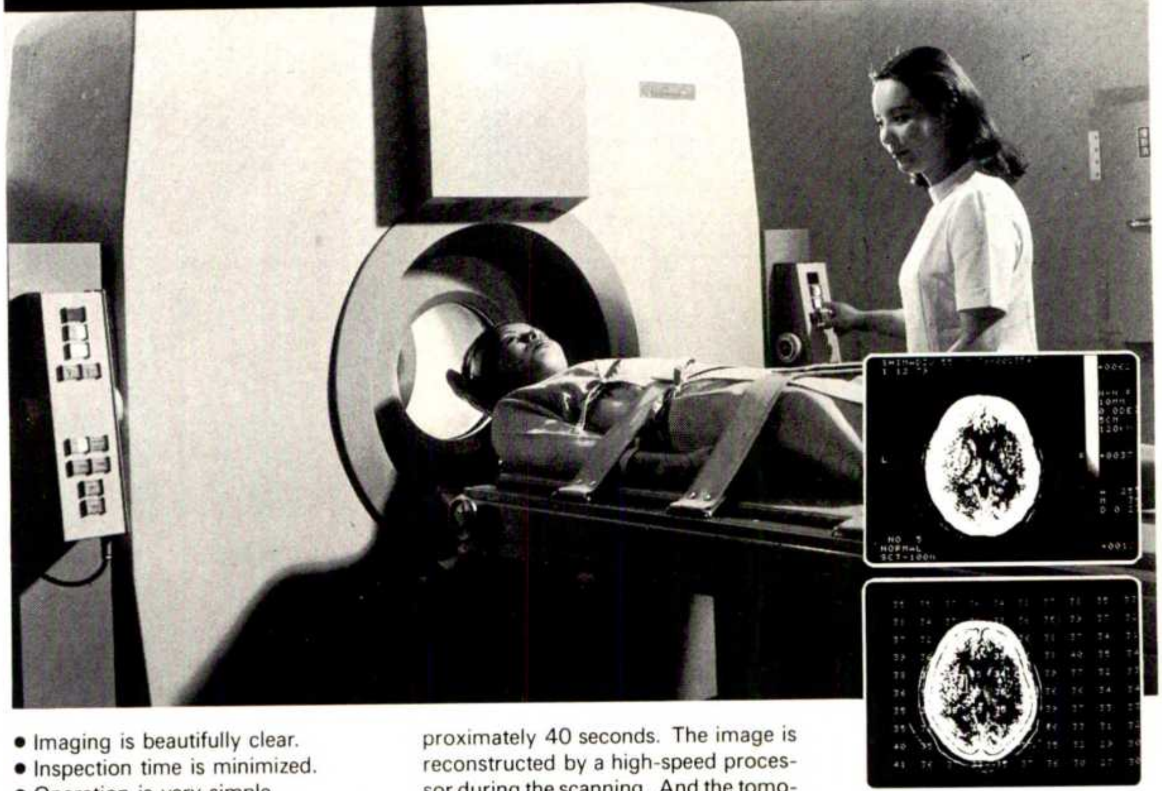
Head Office: Holland, Oldelft Deltronix bv. Den Haag
Fruitweg 9. Tel. (070) 88 89 63
België/Belgique 2100 Deurne, Twee Gezusterslaan 34,
Tel. (031) 24 93 05.

Deutschland D 6300 Giessen Lahn. Postfach 5420.
Tel. (0641) 4 10 49
España Madrid 16. Uruguay 13. Tel. (01) 259 1698
France 91403 Orsay. B.P. 86. Tel. (01) 907 5900
Italia 00146 Roma Via della Vasca Navale 84. Tel. (06) 55 84 311.

Sverige 17206 Sundbyberg 6 Postbox 670. Tel. (08) 98 38 95
Schweiz 8618 Oetwil am See Zelglistrasse 5. Tel. (01) 92 91 318

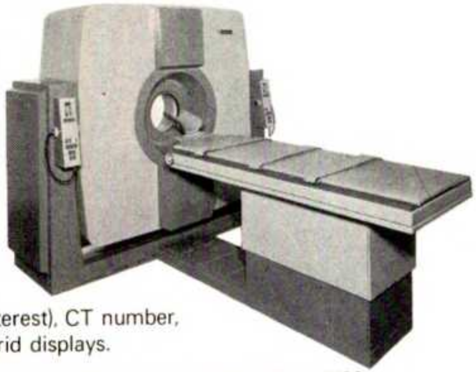
The Shimadzu SCT-100N 40-Second Rapid Scan

Computerized Axial Tomographic Scanner for Neuroradiology



- Imaging is beautifully clear.
- Inspection time is minimized.
- Operation is very simple.
- A wide variety of software is available.
- The entire system is compact.

Computerized tomography has become an essential part of neurological and emergency diagnosis procedures. And easy-to-operate equipment is especially necessary in emergency applications. The Shimadzu computerized axial tomographic scanner for neuroradiology, the SCT-100N, was developed through long engineering experience to meet just such requirements. The SCT-100N completes scanning in only approximately 40 seconds. The image is reconstructed by a high-speed processor during the scanning. And the tomographic image is displayed immediately after the scanning is completed. Image display is by means of a black and white CRT with a 64-level grey scale and 256 × 256 matrix. The main processor, a mini-computer, makes possible a wide range of practical image processing, including ROI (region of interest), CT number, blinking, enlarged and grid displays.



SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
14-5, Uchikanda 1-chome Chiyoda-ku, Tokyo Japan Phone: Tokyo 03-296-2352
Overseas Telex: No.0222-4275 SHMDT J Cable Address: SHIMADZU TOKYO

SHIMADZU (EUROPA) GmbH
4000 Düsseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D

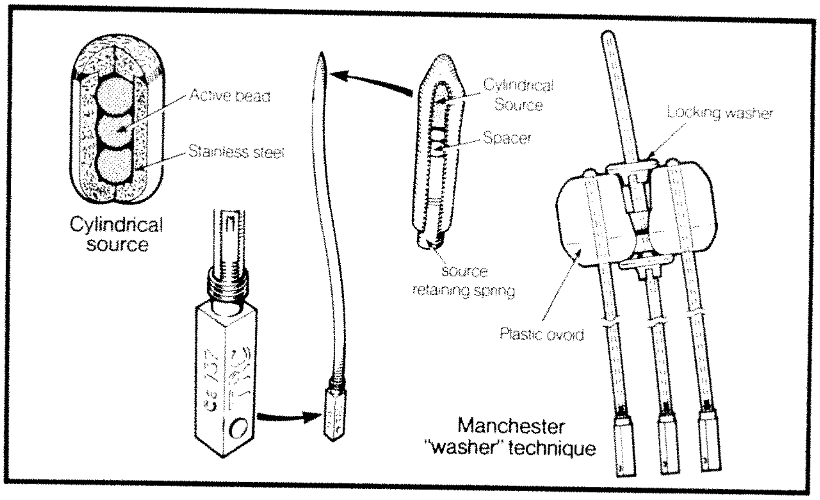
Our Afterloading Systems put brachytherapy right on target

With the addition of our new caesium-137 gynaecological afterloading system, we now supply a comprehensive range of products for intracavitary and interstitial radiotherapy.

Intracavitary radiotherapy

Our caesium-137 "Manchester" afterloading system consists of X-Ray opaque PVC applicators which allow the "washer," "spacer" or "tandem" techniques to be used. The guide tubes are flexible and have a diameter of only 6.3 mm overall. Complete kits are supplied sterilized in packaging designed for maximum convenience in use.

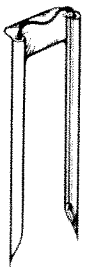
The sources contain glass beads in welded stainless steel capsules assembled into flexible source trains for which special shielded containers are supplied. Iso-dose curves are available for each source train. Individual sources and source trains are also supplied for most of the currently available remote afterloading systems.



Interstitial radiotherapy

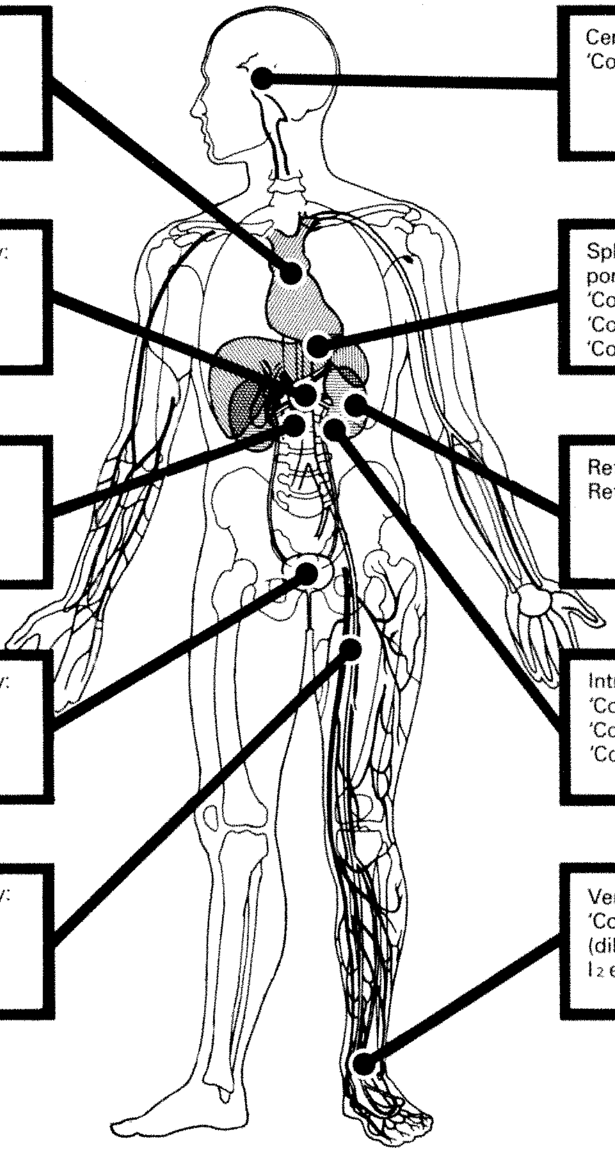
Our iridium-192 flexible wire afterloading systems include complete sets of applicators and accessories for the Pierquin/Paine technique. All accessories for these systems are pre-packed ready for use and sterilized where necessary. Platinum clad iridium-192 wire in 500 mm lengths is readily available in activities up to approximately 0.3 mCi/mm providing exposure rates of up to 0.16 mR per hour at 1 metre.

Iridium-192 "hairpins" and single pins: Thicker platinum coated iridium-192 wire is supplied pre-shaped as "hairpins" and single pins for use with slotted guide needles which are made in stainless steel to the designs of Pierquin and Paine.



The Radiochemical Centre
Amersham

Full information is available on request.
The Radiochemical Centre Limited, Amersham, England. Telephone: 024-04-4444
In the Americas: Amersham Corporation, Illinois 60005. Telephone: 312-593-6300
In W. Germany: Amersham Buchler GmbH & Co KG, Braunschweig. Telephone: 05307-4691
1885



CONRAY
Let us put you fully in the picture about the 'Conray' range of contrast media

Angio-cardiography:
Cardio – 'Conray':
'Conray 420':
'Conray 280'

Abdominal-aortography:
'Conray 280':
'Conray 420':
'Conray 325':
Cardio – 'Conray'

Gastroenterography:
Gastro – 'Conray'

Retrograde cystography:
'Conray 280':
'Conray 420'
(suitably diluted)

Peripheral arteriography:
'Conray 280'

Cerebral angiography:
'Conray 280'

Splenography and
portal venography:
'Conray 280':
'Conray 420':
'Conray 325'

Retrograde pyelography:
Retro – 'Conray'

Intravenous urography:
'Conray 325':
'Conray 420':
'Conray 280'

Venography:
'Conray 280'
(diluted to 150–200 mg
I_2 equivalent)

Conray Contrast Media
(Meglumine and sodium iothalamate)

No matter what your particular requirements may be, there is almost certainly a presentation suitable. If you are in any doubt whatever, contact your May & Baker representative or telephone our Medical Information Department (01-592 3060)

Full information supplied on request

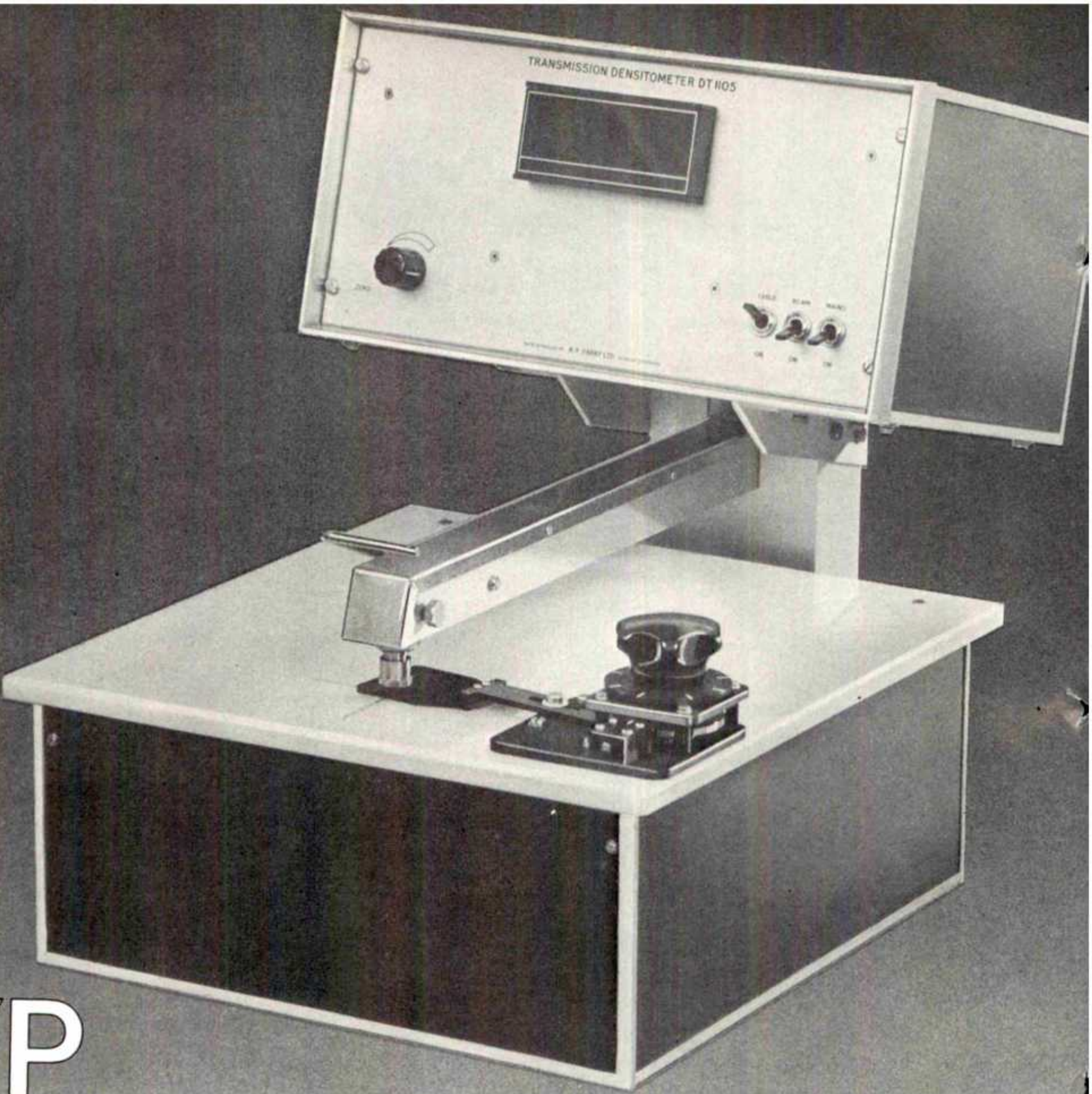
'Conray' is a trade mark of Mallinckrodt Inc.

May & Baker Ltd Dagenham Essex RM10 7XS

M&B May&Baker

A member of the Rhône-Poulenc Group of Companies

MA 7534



RYP

digital transmission densitometer DT 1105

The World standard film badge reader

Used by many hospitals, research establishments and radiological protection services throughout the world.
Gives fast digital indication to density 6 and with an accuracy of 1%. Film pantograph, B.C.D. output and Printer available.

For full information contact:

R.Y. Parry Limited

Kings Road (West),
Newbury, Berks, RG14 5DA.
Telephone: (0635) 46116.

RYP **INSTRUMENTS**

1980, *British Journal of Radiology*, *53*, 1–4

VOLUME 53 NUMBER 625 JANUARY 1980

The British Journal of Radiology

Ultrasonic scanning in suspected ectopic pregnancy

By J. F. Pedersen, M.D.

Ultrasound Laboratory, Department of Obstetrics and Gynaecology YB, University Clinic, Rigshospitalet, Copenhagen

(*Received March 1979 and in revised form June 1979*)

ABSTRACT

A consecutive series of 103 ultrasound examinations for suspected ectopic pregnancy is presented. The positive ultrasound diagnosis of ectopic pregnancy was based on the demonstration of fetal heart activity outside the uterus and was correct in four out of four cases. The exclusion of ectopic pregnancy was correct in 71 out of 72 cases. Among 24 patients with an ultrasound report of possible ectopic pregnancy five patients were confirmed to have an ectopic pregnancy. Three patients were lost to follow-up. An echo-free area centrally in the uterus was seen in four out of nine patients with ectopic pregnancy, and may prove useful as a sign of ectopic pregnancy.

Frequently the diagnosis of ectopic pregnancy is clinically fairly obvious and the patient can be taken directly to laparoscopy and/or operation, laparoscopy being a well-accepted diagnostic modality in this clinical situation (Cibils, 1975). In cases with only mild clinical suspicion, however, a non-invasive means of selecting patients for laparoscopy is desirable.

Few studies have dealt with the value of ultrasonic scanning in suspected ectopic pregnancy (Kobayashi *et al.*, 1969; Kukard and Coetzee, 1974; Calvo *et al.*, 1977; Maklad and Wright, 1978; Lawson, 1978). The present paper reports on a consecutive series of 103 ultrasound examinations in patients with only mild to moderate suspicion of ectopic pregnancy. In clinically obvious cases the patients were managed without recourse to ultrasound scan, usually because the additional delay in treatment was considered unacceptable.

MATERIAL AND METHODS

In a 22 month period 103 ultrasound examinations for suspected ectopic pregnancy were performed. The patients were examined with the full bladder technique (Donald, 1963), using a Nuclear Enterprises Diasonograph (NE 4102), the majority being examined after installation of a scan converter grey scale attachment.

The possible ultrasonic findings are listed in Table I. An intrauterine pregnancy may be found, sometimes associated with a space occupying lesion lateral to the uterus. This is usually an ovarian (lutein) cyst which has given rise to the clinical suspicion. Alternatively, no sign of an intrauterine pregnancy may be detected. If no space occupying lesion is seen lateral to the uterus, or just a simple cyst is demonstrated with a smooth, regular wall and no internal echoes, these examinations, together with those of proven intrauterine pregnancy, are considered negative for ectopic pregnancy.

Adjacent to a non-pregnant uterus a more complex space occupying lesion may be seen, or occasionally an appearance similar to a gestation sac and/or a fetus may be present. Whatever the appearance, if fetal heart activity can be demonstrated within the lesion, the diagnosis must be ectopic pregnancy. However, if no fetal heart activity can be demonstrated within the lesion, we have given a diagnosis of possible ectopic pregnancy. The same diagnosis has been used when an echo-free space is found behind the uterus in the cul de sac, indicating free fluid which, in this clinical situation, is most likely to be blood.

The final diagnosis was obtained at laparoscopy or operation in a minority of the patients, and by follow-up enquiry in the remainder. If no ectopic pregnancy was revealed within two months after the ultrasound examination, the patients are listed as having had no ectopic pregnancy at the time of examination, although spontaneous regression or unrecognized tubal abortion theoretically could have taken place. Three patients, two of them tourists, and all with an ultrasound diagnosis of no sign of ectopic pregnancy were lost to follow-up.

RESULTS

Table I shows the distribution of the findings in 100 ultrasound examinations, where a final diagnosis

TABLE I

ULTRASOUND FINDINGS AND ULTRASOUND DIAGNOSES IN 100 OUT OF 103 EXAMINATIONS FOR SUSPECTED ECTOPIC PREGNANCY. THREE PATIENTS LOST TO FOLLOW-UP

Ultrasound findings in suspected ectopic pregnancy						Ultrasound diagnosis
Intrauterine pregnancy				27	72	No ectopic pregnancy
No intrauterine pregnancy	no adnexal mass			33		
	adnexal mass	simple cyst		12		
		other	−FHA	24		Possible ectopic pregnancy
			+FHA	4		Ectopic pregnancy
			Total	100		

FHA, fetal heart activity.

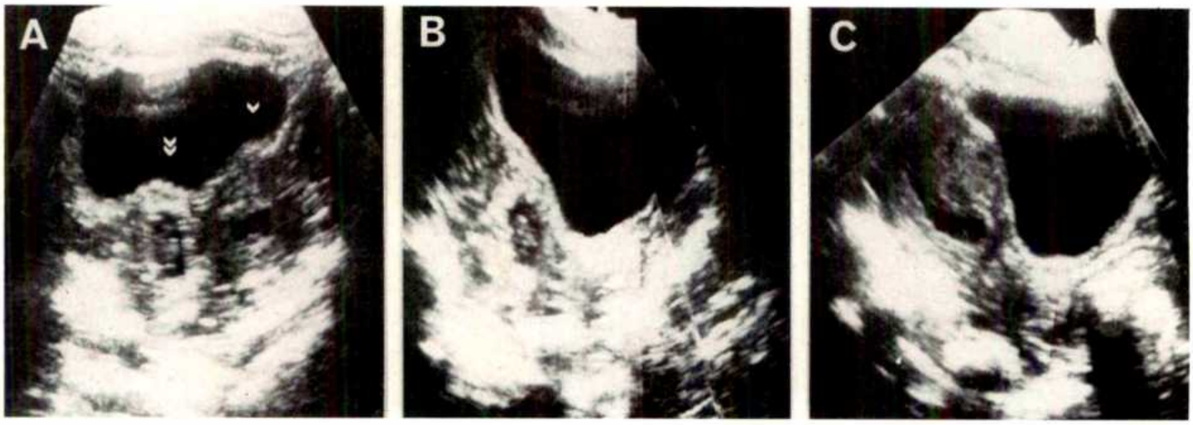


FIG. 1.

Sonograms from patient with ectopic pregnancy. (A) Transverse scan showing uterus with central echo-free area, dislocated towards left (single arrow). To the right of uterus ectopic gestation sac with a 10 mm fetus (double arrow). With the sound-beam directed towards the centre of the fetus, heart movements could be detected. (B) Longitudinal scan through ectopic gestation sac. (C) Longitudinal scan through uterus showing echo-free central area, mimicking a gestation sac.

TABLE II

ULTRASOUND DIAGNOSIS AND FINAL DIAGNOSIS IN 100 EXAMINATIONS FOR SUSPECTED ECTOPIC PREGNANCY

	Final diagnosis		
Ultrasound diagnosis	ectopic	no ectopic	Total
No ectopic pregnancy	1	71	72
Possible ectopic pregnancy	5	19	24
Ectopic pregnancy	4	—	4
Total	10	90	100

is available. Sonograms from one patient with ectopic pregnancy are shown in Fig. 1.

Table II relates the ultrasound diagnosis to the final diagnosis. All four ultrasound reports of ectopic pregnancy were correct. The report of no ectopic pregnancy was correct in 71 of 72 cases, the one error occurring in a patient with a tubal pregnancy, menstrual age seven weeks and six days, which was misinterpreted as a slightly enlarged ovary. There were five cases of ectopic pregnancy among the 24 reported as possible ectopic pregnancy.

DISCUSSION

In suspected ectopic gestation the ultrasonic demonstration of an intrauterine pregnancy, sometimes associated with an ovarian cyst, will clarify the situation. The likelihood of a co-existing ectopic pregnancy is one in 30 000, but probably much

TABLE III

DIAGNOSTIC VALUE OF ULTRASONIC SCANNING IN SUSPECTED ECTOPIC PREGNANCY. THE FIGURES FROM THE LITERATURE ARE REARRANGED TO EXPRESS THE PREDICTIVE VALUE OF A POSITIVE AND A NEGATIVE ULTRASOUND DIAGNOSIS

Author	True positive	Ectopics in "possible" group	True negative
Kobayashi *et al.* (1969)	16/21 (76%)	—	13/18 (72%)
Kukard and Coetzee (1974)	12/22 (55%)	—	23/26 (88%)
Calvo *et al.* (1977)	15/17 (88%)	9/24	34/34 (100%)
Maklad and Wright (1978)	11/12 (92%)	—	23/24 (96%)
Lawson (1978)	20/28 (71%)	—	201/207 (97%)
Present paper	4/4 (100%)	5/24	71/72 (99%)

greater in patients treated with ovulatory induction drugs (Berger and Taylor, 1972). It is mandatory to demonstrate a fetus within the gestation sac and not just the sac, since the latter may be mimicked by the echo-free area centrally in the uterus, often seen in ectopic pregnancy (Fig. 1). Likewise, demonstration of an empty uterus without an adnexal mass, or associated with a simple ovarian cyst virtually excludes the presence of an ectopic pregnancy. However, since ectopic pregnancy is a potentially life threatening condition, an ultrasound report stating that there is no evidence of an ectopic pregnancy should not be relied on if strong clinical suspicion persists.

The problems arise with more complex adnexal masses. These may look almost like a normal gestation sac, with a structure inside looking like a fetus. If fetal heart activity can be demonstrated in the fetus-like structure, the diagnosis of ectopic pregnancy is certain. If fetal heart activity cannot be detected we have chosen to report these cases as possible ectopic pregnancy, even if the lesion looks exactly like a gestation sac with a fetus, as was actually the case in one of the five ectopic pregnancies in this group. At operation it became clear that the fetus, approximately seven weeks of age, had been dead for some time. Another live fetus, with a menstrual age of 6½ weeks, could not be confirmed by ultrasound at the initial scan since fetal heart activity is not routinely demonstrable at this stage of gestation (Robinson and Shaw-Dunn, 1973). At repeat examination one week later the fetal heart activity could be demonstrated at the location suspected at the earlier scan.

Detection of fetal heart activity outside the uterus as a definitive sign of ectopic pregnancy was possible in less than half of the cases. This sign has generally not been evaluated in other series, probably because the equipment used was less suited for fetal heart activity detection. Kobayashi *et al.* (1969) introduced uterine enlargement with amorphous intrauterine echoes as a diagnostic criterion. In recent reports Maklad and Wright, 1978; Brown *et al.*, 1978; Schoenbaum *et al.*, 1978) and in the present series this sign has proven inconstant and unspecific. In contrast an echo-free area centrally in the uterus, resembling an empty gestation sac, but without the expected denser halo of echoes, was seen in four of our nine patients with ectopic pregnancy, but in none of the remainder (Fig. 1). A similar finding is described by Schoenbaum *et al.* (1978) in three out of 15 cases and by Lawson (1978) in one out of 26 cases of ectopic pregnancy. This appearance is probably caused by decidual reaction and bleeding. Apart from representing a potential pitfall it may actually prove useful as an indicator of ectopic pregnancy.

The referring physician will want to know the reliability of the ultrasound diagnosis. We have therefore arranged our figures to indicate the number of correct positive and negative ultrasound diagnoses. For comparison the results from other reports have been recalculated when possible (Table III). Improved equipment, especially the introduction of grey scale scanning, may explain the good results of recent reports. The predictive value of a confident positive or negative ultrasound diagnosis is apparently now very high (Table III). However, the predictive value of an equivocal positive report is low because of difficulties in differentiating between adnexal inflammatory disorders, ovarian lesions and ectopic pregnancies with a dead fetus. It may improve with experience and with further advances in equipment design.

REFERENCES

BERGER, M. J. and TAYLOR, M. L., 1972. Simultaneous intrauterine and tubal pregnancies following ovulation induction. *American Journal of Obstetrics and Gynecology*, *113*, 812–813.

BROWN, T. L., FILLY, R. A., LAING, F. C. and BARTON, J., 1978. Analysis of ultrasonographic criteria in the evaluation for ectopic pregnancy. *American Journal of Roentgenology*, *131*, 967–971.

Calvo, C. C., Peman, F. C., Garcia, J. M. J. and Hernandez, J. P., 1977. Two-dimensional echography with a real-time scanner in extrauterine pregnancy. *Geburtshilfe und Frauenheilkunde*, *37*, 393–405.

Cibils, L. A., 1975. *Gynecologic Laparoscopy* (Lea & Febiger, Philadelphia), p. 60.

Donald, I., 1963. The use of ultrasonics in the diagnosis of abdominal swellings. *British Medical Journal*, *2*, 1154–1155.

Kobayashi, M., Hellman, L. M. and Filisti, L. P., 1969. Ultrasound. An aid in the diagnosis of ectopic pregnancy. *American Journal of Obstetrics and Gynecology*, *103*, 1131–1140.

Kukard, R. F. P. and Coetzee, M., 1974. A comparison between ultrasonic and clinical reliability in early pregnancy complications. *South African Medical Journal*, *48*, 2109–2112.

Lawson, T. L., 1978. Ectopic pregnancy: criteria and accuracy of ultrasonic diagnosis. *American Journal of Roentgenology*, *131*, 153–156.

Maklad, N. F. and Wright, C. H., 1978. Grey scale ultrasonography in the diagnosis of ectopic pregnancy. *Radiology*, *126*, 221–225.

Robinson, H. P. and Shaw Dunn, J., 1973. Fetal heart rates as determined by sonar in early pregnancy. *The Journal of Obstetrics and Gynaecology of the British Commonwealth*, *80*, 805–809.

Schoenbaum, S., Rosendorf, L., Kappelman, N. and Rowan, R. T., 1978. Gray-scale ultrasound in tubal pregnancy. *Radiology*, *127*, 757–761.

Book review

1979 Year Book of Diagnostic Radiology. Editor W. M. Whitehouse and associate editors, pp. 448. 1979 (Year Book Medical Publishers, Chicago, London), £24·50.
ISBN 0-8151-9325-4

"It is again apparent that we are living in an exciting and rapidly changing era in diagnostic radiology . . . applied technology . . . interactive social and political scene . . ." Here we go again, you may think from the preface to this year's book. But not so: with the obligatory trite phrases out of the way, the current volume seems even better than before. The selection of papers is interesting, the editorial comments crisp, the illustrations superb. How do you use the series? Sometimes I misuse it as a gossip column to check up on friends and enemies (who's in, who's out), at others it is the key to locating a dimly remembered reference (wasn't it about 1971?). It is also the ideal holiday book for a rapid gallop around the fields I should have ploughed in the library week by week this last year.

There are the expected exotica: did you know about gamekeeper's thumb, pulmonary barotrauma in scuba divers, rocket propellant inhalation in the Apollo-Soyuz astronauts? Best of all, there is solid paper on paper for everyday radiological practice, and I am grateful for much that I would have missed otherwise.

The book's chapter organization is interesting, reflecting our own difficulties. Are we technique specialists covering all clinical fields (ultrasound, angiography), or diagnostic physicians along clinical compartments (neuroradiology, gastro-intestinal tract etc.)? The answer matters, I think, because only the second sort of radiologist can act as true consultant, speaking the clinician's language. So I was pleased not to see a chapter on CT: instead the technique crops up throughout the clinically orientated sections.

The book even contains occasional glimpses of the critical stance needed for the 1980s, like "Limitations of angiographic differential diagnosis in major hepatic processes"—required reading for anyone performing hepatic angiography, says the editor. It is a good buy.

Thomas Sherwood.

1980, *British Journal of Radiology*, *53*, 5–11 JANUARY 1980

The measurement of effective photon energy and "linearity" in computerized tomography

By D. R. White, M.Sc., Ph.D.

Radiation Physics Department, St. Bartholomew's Hospital, 13 Bartholomew Close, London EC1A 7BE

and R. D. Speller, B.Sc., Ph.D.

Department of Physics as Applied to Medicine, Middlesex Hospital Medical School, Cleveland Street, London W1P 6DB

(*Received September 1978 and in revised form May 1979*)

ABSTRACT

Two liquid systems have been developed for the measurement of effective photon energy (E_{eff}) and "linearity" in computerized tomography (CT). A group of sixteen "keV liquids" enables an E_{eff} to be rapidly determined, by comparing the CT numbers of the specially formulated organic liquid mixtures with similar data for water. The "linearity" of the CT scanner, relating CT numbers to linear attenuation coefficients, may be investigated using 14 selected organic "linearity liquids". Details of these systems, together with some typical results, are presented.

The result of computerized image reconstruction is a matrix of data that relates to some physical property of the object being imaged. With computer assisted X-ray transmission tomography, such data appear to correlate well with the total linear attenuation coefficient (μ) of each matrix element of the object (McCullough, 1975; Kiker *et al.*, 1976; Rutherford *et al.*, 1976). However, in order to relate the reconstructed value of the picture element (pixel) of a CT image to a linear attenuation coefficient, it is necessary to have an estimate of the effective energy (E_{eff}) of the X-ray beam.

The proliferation of these scanning systems in both clinical and research establishments has made greater demands upon their quantitative behaviour. For example, checking the "linearity" of the system, *i.e.* correlating the CT numbers with estimated μ-values, is desirable if the data are to be used in dose calculations for radiotherapy treatment planning.

In this paper, a technique is presented for accurately assessing both the effective photon energy and the "linearity" of any CT machine. The method, which uses a set of specially prepared liquid mixtures (Speller and White, 1977), may be applied to brain or whole-body scanners. The composition and properties of the liquid mixtures, together with some typical experimental results, will be given in subsequent sections.

MATERIALS AND METHODS

McCullough (1975) has shown that if energy fluence ψ is being measured, a polychromatic X-ray beam, after transversing a path length x, has a local attenuation coefficient, μ_ψ, given by

$$\mu_\psi = \frac{\delta\psi/\delta x}{\psi}$$

which is identical to the attenuation coefficient averaged over the local differential spectra. McCullough indicates that a measurement of μ_ψ permits the specification of an effective energy, being that monoenergetic photon-beam energy which has an attenuation coefficient equal to μ_ψ of the polychromatic beam.

Since all corrections to the reconstructed pixel values performed by commercial CT scanners appear to be based upon pixel position, comparisons between adjacent areas of the image will be indicative of changes in local attenuation coefficients. In order to determine the effective energy at a particular position within a phantom, it is only necessary to compare the CT numbers of two materials of known composition scanned sequentially at that position. To simplify the analysis test materials may be used, each having, at specific photon energies, the same (narrow beam) μ-value as a standard material. If the number of matching energy points adequately covers the expected energy range (*e.g.* 60–90 keV, in 2 keV increments), selecting the test material that has the same CT number as the standard material will immediately yield the effective energy (E_{eff}.). Once this energy has been determined, the μ-values for the complete range of test materials may be calculated so that the relationship between CT number and μ may be established. The test materials will, therefore, enable both effective energy and "linearity" to be investigated.

In this study water is chosen as the standard liquid and test materials are formulated from suitable organic liquids which have CT numbers spanning those found in the human body. To produce the required effect, the μ-values of the liquid mixture must vary with energy more rapidly than similar data for water, and in addition the curves of μ versus energy must intersect at specific energies within the interval 60–90 keV. This may readily be achieved with two-component mixtures of organic liquids, made up of a primary liquid having μ-values (μ_p) below those of water (μ_w), and a secondary liquid having μ-values (μ_s) above μ_w. Furthermore, μ_s, with its larger photoelectric component, must vary more rapidly than μ_w with respect to photon energy. With these conditions satisfied, the fractional proportions by volume of the primary and secondary components (φ_p, φ_s) may be calculated for each matching energy point by the relationship.

$$\mu_w = \varphi_p\mu_p + \varphi_s\mu_s \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Table I lists some "keV liquid" systems that fulfil these attenuation requirements. The components must also be available as high purity liquids and be capable of being dispensed with high precision. (Precise dispensing becomes difficult if small quantities of secondary component, below 1% by volume, have to be added to the primary liquid.)

The combination which has been found in practice to have the best performance is ethanol and carbon tetrachloride, and 16 formulated liquid mixtures matching the μ-values of water from 60–90 keV are

TABLE I

Possible "keV liquid" systems

Primary liquid	Secondary liquid
Ethanol	Carbon tetrachloride
Ethanol	Ethyl iodide
Methanol	Carbon tetrachloride
Propanol	Carbon tetrachloride
Hexane	Carbon tetrachloride

TABLE II

Recommended "keV liquid" system

	Constituents, % by volume	
"keV liquid"	Ethanol	Carbon tetrachloride
KEV1/60	90.68	9.32
KEV1/62	90.19	9.81
KEV1/64	89.68	10.32
KEV1/66	89.18	10.82
KEV1/68	88.67	11.33
KEV1/70	88.15	11.85
KEV1/72	87.64	12.36
KEV1/74	87.12	12.88
KEV1/76	86.61	13.39
KEV1/78	86.09	13.91
KEV1/80	85.58	14.42
KEV1/82	85.08	14.92
KEV1/84	84.58	15.42
KEV1/86	84.09	15.91
KEV1/88	83.60	16.40
KEV1/90	83.12	16.88

Note. The density of mixtures of ethanol and carbon tetrachloride has been verified to be that expected for a simple mixture.

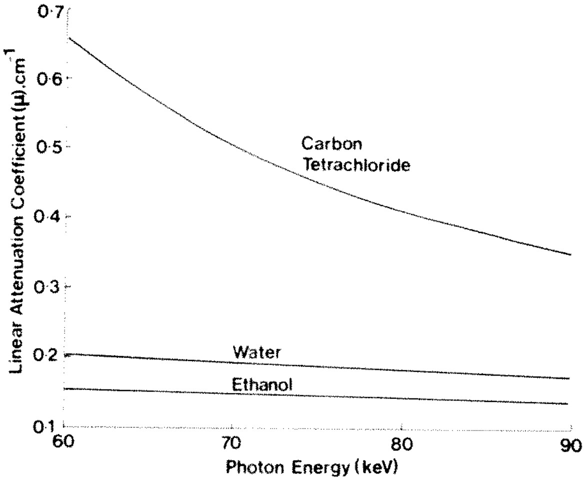


Fig. 1.

The photon attenuation characteristics of ethanol, water and carbon tetrachloride.

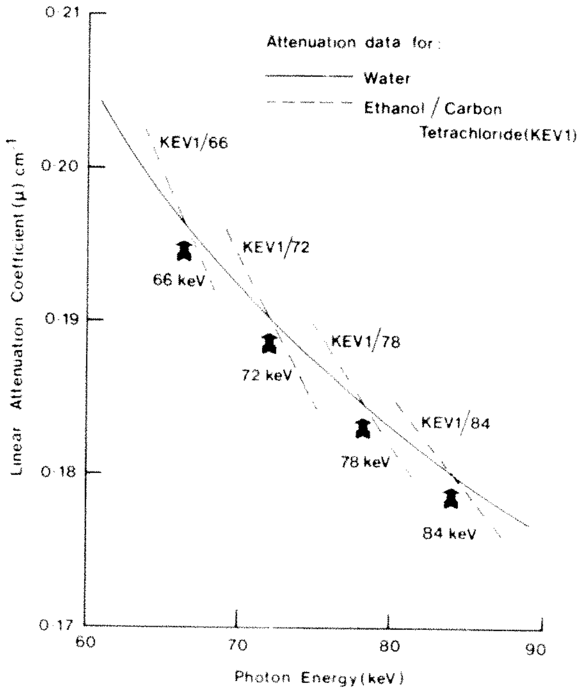


Fig. 2.

The performance of "keV liquid", KEV1, over the photon energy range 60–90keV.

listed in Table II. Each "keV liquid" is designated by the code "KEV1", followed by the photon energy, in keV, at which the μ-values for the "keV liquid" match those of water. For example, "KEV1/60", denotes that mixture of ethanol and carbon tetrachloride that has the same μ-value as water at 60 keV. In Table II the proportions by volume of the two components of "KEV1" are given, calculated from equation (1).

The suitability of this system is illustrated in Figs. 1 and 2. In Fig. 1, μ-values for ethanol, water and carbon tetrachloride are plotted over the energy interval 60–90 keV. It can be seen that the μ-values of the organic liquids chosen bracket those of water, with the data for carbon tetrachloride having a steeper slope. In Fig. 2 the way in which the curves of μ-values versus photon energy for the "keV liquids" intersect the curve for water is illustrated for four representative systems (KEV1/66, KEV1/72, KEV1/78 and KEV1/84). Each "keV liquid" shows ~1% difference in μ-value with respect to water for a 2 keV variation from the matching energy points, a variation readily discernible in CT images. All of the μ-values presented here and, indeed, elsewhere in this paper, are calculated from techniques described in detail by White and Fitzgerald (1977), in which elemental photon cross sections of Hubbell (1969) and Storm and Israel (1970) are used together with a polynomial fitting procedure similar to that introduced by McMaster *et al.* (1969). For the calculations, ethanol (C_2H_6O) is assumed to contain 0.3% by volume of water and to have a mass density of 0.790 g/cm^3, carbon tetrachloride (CCl_4) 1.594 g/cm^3 and water a value of 0.998 g/cm^3 (all at 20°C). The uncertainties in the attenuation data employed are approximately 1%, which results in an error in E_{eff} of 2–3 keV.

The series of "keV liquids" may be used to establish the "linearity" of a CT scanner, by determining the CT numbers of all of the 16 liquid mixtures and, knowing the effective photon energy, plotting the derived CT numbers versus calculated μ-values. The "linearity" graph may be confirmed and, if necessary, extended to higher μ-values by measuring the CT numbers of selected organic liquids. The attenuation properties of all of the available relevant Analar organic liquids have been calculated and the 14 most suitable "linearity liquids" are listed in Table III. Complete tabulations of μ-values for the energy range 60–90 keV for both systems of liquids are given in Tables IV and V.

RESULTS

To investigate the response of the "keV liquids", a selection of eight liquids (KEV1/60 to KEV1/74) covering the photon energy range 60–74 keV, contained in 1.2 cm diameter polypropylene tubes, were placed in a 20 cm diameter water-filled Perspex container. The phantom was then scanned on a CT1010 EMI scanner at peak voltages of 110, 115, 120, 125 and 130 kV and reconstructed on a 160 × 160 matrix. Figure 3 shows the scans obtained, the added arrows indicating where the "keV liquids" match water, and consequently the effective photon energies which range from 62–69 keV. It is evident that changes of 5kVp are readily detected visually with the system.

Linearity tests were performed on a CT5005 EMI scanner by placing sequentially a water sample, individual "keV liquids" and "linearity liquids" contained in 2.8 cm diameter polypropylene tubes into three types of epoxy-resin based solid phantoms (White *et al.*, 1977). The latter were a 33 cm diameter and two 20 cm diameter phantoms (one with a 4 mm simulated cortical bone ring) representing an equivalent water volume. The 20 cm diameter phantoms, simulating adult skulls, were scanned at 120 kV and the 33 cm diameter phantom, simulating the adult thorax/abdomen, at 140 kV, and both were reconstructed on a 160 × 160 high-precision reconstruction mode using 2085/VO1 EMI software. After each scan the mean CT number and standard deviation of the liquid were determined within a radius of 5 pixels (total 70 pixels). Figure 4 shows the CT number data obtained plotted against linear attenuation coefficients calculated for the effective photon energy derived by a comparison of the CT numbers for water and the "keV liquids". The three graphs are seen to be essentially linear over the range of CT numbers considered (−100 to +120) with the

TABLE III

RECOMMENDED LINEARITY LIQUIDS

Liquid	Chemical formula	Mass density (g/cm^3)
Ethyl acetate	$C_4H_8O_2$	0.900
Ethoxyethanol	$C_4H_{10}O_2$	0.930
Dimethylformamide	C_3H_7NO	0.949
Acetylacetone	$C_5H_8O_2$	0.973
Benzaldehyde	C_7H_6O	1.045
Hydrazine hydrate	H_6N_2O	1.033
Ethanediol	$C_2H_6O_2$	1.113
Glycerol	$C_3H_8O_3$	1.260
Chlorobenzene	C_6H_5Cl	1.106
Dimethyl sulphoxide	C_2H_6OS	1.100
Dichlorobenzene	$C_6H_4Cl_2$	1.305
Dichloroethane	$C_2H_4Cl_2$	1.253
Trichloroethane	$C_2H_3Cl_3$	1.333
Dichloromethane	CH_2Cl_2	1.324

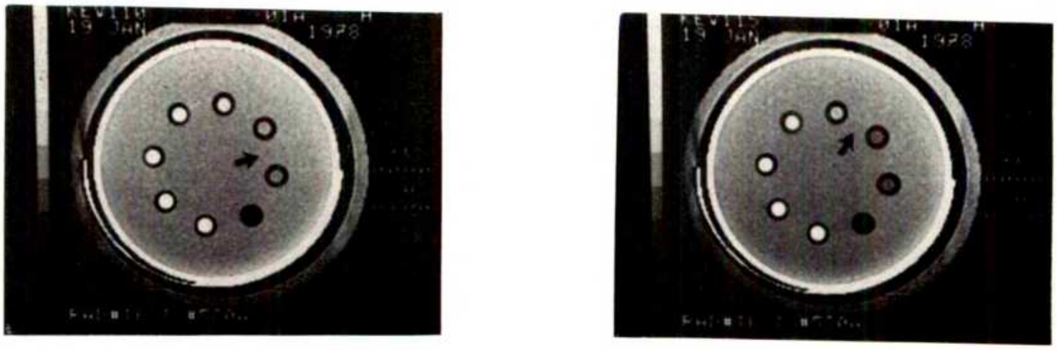
TABLE IV

LINEAR ATTENUATION COEFFICIENTS FOR KEV LIQUIDS

keV liquid	Linear attenuation coefficients (μ) cm ^{1}																														
	Energy (keV)																														
	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90
KEV1/60	**.205**	.203	.200	.198	.195	.193	.191	.189	.187	.185	.183	.182	.180	.179	.177	.176	.174	.173	.172	.171	.169	.168	.167	.166	.165	.164	.163	.162	.161	.161	.160
KEV1/62	.208	.205	**.202**	.200	.197	.195	.193	.191	.189	.187	.185	.183	.182	.180	.179	.177	.176	.175	.173	.172	.171	.170	.169	.167	.166	.165	.164	.164	.163	.162	.161
KEV1/64	.210	.207	.205	.202	**.200**	.197	.195	.193	.191	.189	.187	.185	.184	.182	.180	.179	.177	.176	.175	.173	.172	.171	.170	.169	.168	.167	.166	.165	.164	.163	.162
KEV1/66	.213	.210	.207	.204	.202	.199	**.197**	.195	.193	.191	.189	.187	.185	.184	.182	.180	.179	.178	.176	.175	.174	.172	.171	.170	.169	.168	.167	.166	.165	.164	.163
KEV1/68	.216	.212	.209	.207	.204	.201	.199	.197	**.195**	.193	.191	.189	.187	.185	.184	.182	.180	.179	.178	.176	.175	.174	.172	.171	.170	.169	.168	.167	.166	.165	.164
KEV1/70	.218	.215	.212	.209	.206	.204	.201	.199	.197	.194	**.192**	.190	.189	.187	.185	.184	.182	.180	.179	.178	.176	.175	.174	.173	.171	.170	.169	.168	.167	.166	.165
KEV1/72	.221	.217	.214	.211	.208	.206	.203	.201	.199	.196	.194	.192	**.190**	.189	.187	.185	.184	.182	.181	.179	.178	.176	.175	.174	.173	.172	.170	.169	.168	.167	.166
KEV1/74	.223	.220	.217	.214	.211	.208	.205	.203	.200	.198	.196	.194	.192	.190	**.188**	.187	.185	.183	.182	.181	.179	.178	.176	.175	.174	.173	.172	.171	.170	.169	.168
KEV1/76	.226	.222	.219	.216	.213	.210	.207	.205	.202	.200	.198	.196	.194	.192	.190	.188	**.187**	.185	.183	.182	.181	.179	.178	.177	.175	.174	.173	.172	.171	.170	.169
KEV1/78	.229	.225	.221	.218	.215	.212	.209	.207	.204	.202	.200	.198	.196	.194	.192	.190	.188	.186	**.'85**	.183	.182	.180	.179	.178	.177	.175	.174	.173	.172	.171	.170
KEV1/80	.231	.227	.224	.220	.217	.214	.212	.209	.206	.204	.202	.199	.197	.195	.193	.191	.190	.188	.186	.185	**.183**	.182	.182	.179	.178	.177	.175	.174	.173	.172	.171
KEV1/82	.234	.230	.226	.223	.220	.216	.214	.211	.208	.206	.203	.201	.199	.197	.195	.193	.191	.189	.188	.186	.185	.183	**.182**	.180	.180	.178	.177	.175	.174	.173	.172
KEV1/84	.236	.232	.229	.225	.222	.219	.216	.213	.210	.208	.205	.203	.201	.198	.196	.195	.193	.191	.189	.188	.186	.184	.183	.182	**.180**	.179	.178	.176	.175	.174	.173
KEV1/86	.239	.235	.231	.227	.224	.221	.218	.215	.212	.209	.207	.204	.202	.200	.198	.196	.194	.192	.191	.189	.187	.186	.184	.183	.181	.180	**.178**	.178	.176	.175	.174
KEV1/88	.241	.237	.233	.229	.226	.223	.220	.217	.214	.211	.209	.206	.204	.202	.200	.198	.196	.194	.192	.190	.189	.187	.186	.184	.183	.181	.180	.179	**.178**	.176	.175
KEV1/90	.244	.239	.235	.232	.228	.225	.221	.218	.216	.213	.210	.208	.205	.203	.201	.199	.197	.195	.193	.192	.190	.188	.187	.185	.184	.182	.181	.180	.179	.177	**.176**

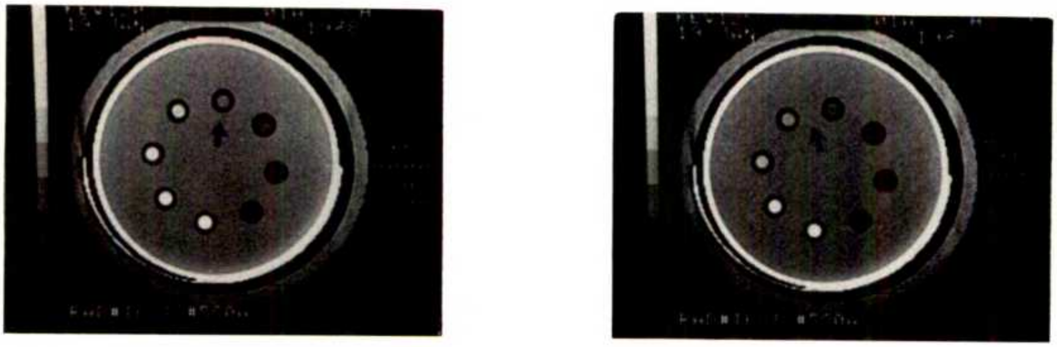
TABLE V
LINEAR ATTENUATION COEFFICIENTS FOR LINEARITY LIQUIDS

	Linear attenuation coefficients (μ) cm ^{1}																														
	Energy (keV)																														
Linearity liquid	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90
Ethylacetate	.175	.174	.173	.172	.171	.170	.169	.169	.168	.167	.166	.165	.165	.164	.163	.162	.162	.161	.161	.160	.159	.159	.158	.158	.157	.156	.156	.155	.155	.154	.154
Ethoxyethanol	.184	.183	.182	.181	.180	.179	.178	.177	.176	.175	.174	.174	.173	.172	.171	.171	.170	.169	.169	.168	.167	.167	.166	.166	.165	.164	.164	.163	.163	.162	.162
Dimethyl Formamide	.185	.183	.182	.181	.180	.179	.179	.178	.177	.176	.175	.174	.174	.173	.173	.172	.171	.170	.170	.169	.168	.168	.167	.166	.166	.165	.165	.164	.164	.163	.163
Acetylacetone	.187	.186	.185	.184	.183	.182	.181	.180	.179	.178	.178	.177	.176	.175	.174	.174	.173	.172	.172	.171	.170	.170	.169	.168	.168	.167	.167	.166	.166	.165	.165
Benzaldehyde	.195	.194	.192	.191	.191	.190	.189	.188	.187	.186	.185	.184	.184	.183	.182	.181	.181	.180	.179	.179	.178	.177	.177	.176	.176	.775	.174	.174	.173	.173	.172
Hydrazine Hydrate	.209	.207	.206	.205	.204	.202	.201	.200	.199	.198	.197	.196	.195	.194	.193	.193	.192	.191	.190	.189	.189	.188	.187	.187	.186	.185	.185	.184	.183	.183	.182
Ethanediol	.220	.219	.217	.216	.215	.214	.212	.211	.210	.209	.208	.207	.206	.205	.204	.203	.202	.202	.201	.200	.199	.198	.198	.197	.196	.195	.195	.194	.193	.193	.192
Glycerol	.248	.246	.244	.243	.241	.240	.239	.237	.236	.235	.234	.233	.232	.230	.229	.228	.227	.226	.225	.225	.224	.223	.222	.221	.220	.219	.219	.218	.217	.216	.216
Chlorobenzene	.292	.287	.282	.277	.272	.268	.264	.260	.256	.252	.249	.246	.243	.240	.237	.234	.232	.229	.227	.225	.223	.221	.219	.217	.215	.213	.212	.210	.208	.207	.205
Dimethyl Sulphoxide	.312	.306	.300	.294	.289	.284	.280	.276	.271	.268	.264	.260	.257	.254	.251	.248	.245	.242	.240	.237	.235	.233	.231	.229	.227	.225	.223	.221	.219	.218	.216
Dichlorobenzene	.399	.389	.381	.372	.365	.357	.350	.344	.337	.332	.326	.321	.316	.311	.306	.302	.298	.294	.290	.286	.283	.280	.276	.273	.271	.268	.265	.262	.260	.257	.255
Dichloroethane	.462	.449	.437	.426	.415	.405	.396	.387	.379	.371	.363	.356	.349	.343	.337	.331	.325	.320	.315	.310	.306	.301	.297	.293	.289	.286	.282	.279	.275	.272	.269
Trichloroethane	.516	.501	.487	.474	.461	.450	.439	.428	.418	.409	.400	.392	.384	.377	.369	.363	.356	.350	.344	.339	.333	.328	.323	.319	.314	.310	.306	.302	.298	.294	.291
Dichloromethane	.526	.510	.496	.482	.469	.457	.446	.435	.425	.415	.406	.397	.389	.381	.374	.367	.360	.354	.348	.342	.337	.331	.326	.321	.317	.312	.308	.304	.300	.296	.293
Water	.205	.204	.202	.201	.200	.198	.197	.196	.195	.194	.192	.191	.190	.189	.188	.188	.187	.186	.185	.184	.183	.182	.182	.181	.180	.180	.179	.178	.178	.177	.176



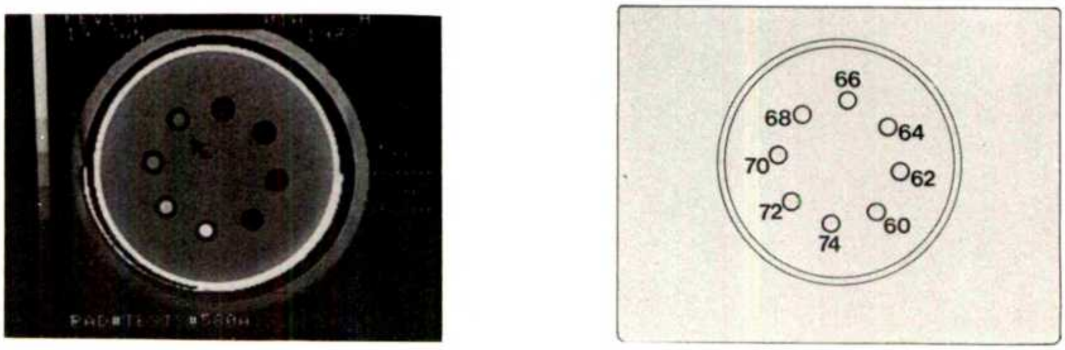
110 kV$_p$; $E_{eff}=63$ keV

115 kV$_p$; $E_{eff}=65$ keV



120 kV$_p$; $E_{eff}=66$ keV

125 kV$_p$; $E_{eff}=67$ keV



130 kV$_p$; $E_{eff}=68$ keV

"keV liquid" arrangement

FIG. 3.

Scans of keV liquids in tubes within a 20 cm diameter water filled Perspex container, using a CT1010 scanner.

data from the "keV liquids" and "linearity liquids" comparing adequately.

Linear relationships of the form: $\mu = a_0 + a_1$ (CT number) fitted by the method of least squares to the data presented in Fig. 4 give the values of a_1, a_2 and as the correlation coefficient, r^2 as outlined below.

A. 33 cm phantom, 140 kVp, $E_{eff}=79$ keV

$$a_0 = 0.184$$
$$a_1 = 3.97 \times 10^{-4}$$
$$r^2 = 0.999$$

B. 20 cm phantom (+4 mm bone), 120 kVp, $E_{eff}=70$ keV

$$a_0 = 0.194$$
$$a_1 = 4.02 \times 10^{-4}$$
$$r^2 = 0.999$$

C. 20 cm phantom (no bone), 120 kVp, $E_{eff}=67$ keV

$$a_0 = 0.200$$
$$a_1 = 3.98 \times 10^{-4}$$
$$r^2 = 0.999$$

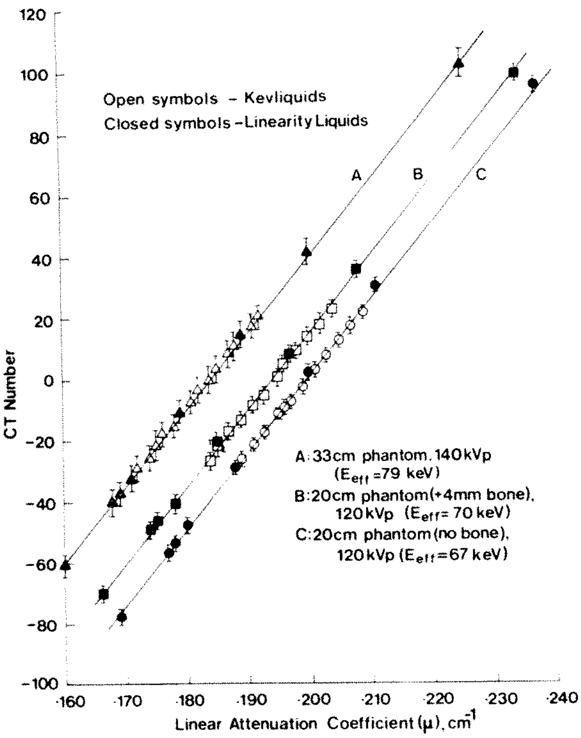


FIG. 4.

"Linearity" plots (CT number versus linear attenuation coefficient) for a CT5005 scanner. The error bars are standard deviations for samples of 70 pixels.

DISCUSSION

To obtain accurate and reproducible results with these liquid systems, high purity liquids must always be used and, in the case of "keV liquids", be carefully dispensed using high quality dispensing equipment. In addition, as the mass densities quoted for both "keV liquids" and "linearity liquids" relate to a temperature of 20°C, significant departures from this value will cause changes in μ-values that must be evaluated.

Care must always be exercised with the storage of organic liquids. During use, the liquids should be contained in stoppered containers to minimize evaporation. Long-term storage should preferably be in amber-coloured glass bottles, having all-glass (or PTFE) stoppers or screw-caps with PTFE liners.

The range of suitable materials for containing organic liquids in phantoms during scanning is limited, and for short-term storage polypropylene tubes and containers appear to be the most appropriate material. (Another advantage of polypropylene is that L-shaped tubes may easily be fabricated in which, if the top of the vertical section of the "L" contains the stopper and the horizontal part is within the scanned volume, trapped air will always be far away from the area of interest and will not be a problem.)

Certain of the "linearity liquids" must not be allowed to come into contact with the eyes or the skin and the manufacturers' instructions regarding safety should always be followed.

A comparison of the measured E_{eff} data presented in this paper with theoretical data (McCullough, 1977) shows good agreement (within 2 keV) with the 20 cm diameter phantoms and appears to confirm that the E_{eff} calculated using energy fluence data is more appropriate to these scanners than the E_{eff} values derived from photon fluence or exposure spectra. With the 33 cm phantom the measured E_{eff} is within 4 keV of the calculated values.

In practice it has been found that the "keV liquid" system, KEV1, is adequate for both effective photon energy and "linearity" determinations, as long as initial checks on the accuracy of the dispensing using selected "linearity liquids" are made on fresh batches of "keV liquids". The "linearity liquids" are convenient for these checks and are particularly useful if a "linearity" relationship extending to high CT numbers is required. Together, these liquid systems can rapidly provide quantitative data over the important clinical range of CT numbers on all types of CT scanners.

REFERENCES

HUBBELL, J. H., 1969. Photon cross sections, attenuation coefficients and energy absorption coefficients from 10 keV to 100 GeV. National Bureau of Standards. NSRDS-NBS 29.

KIKER, W., HINZ, T. W., and LEDLEY, R. S., 1976. Variation of Acta Scanner numbers with the physical properties of the scanned material. *Medical Physics 3*, 42–44.

MCCULLOUGH, E. C., 1975. Photon attenuation in computed tomography, *Medical Physics, 2*, 307–320.
1977. Private communication.

MCMASTER, W. H., KERR DEL GRANDE, N., MALLETT, J. H., and HUBBELL, J. H., 1969. Compilation of X-ray cross sections. UCRL-50174. Sec. II, Rev. 1.

RUTHERFORD, R. A., PULLAN, B. R., and ISHERWOOD, I., 1976. Measurement of effective atomic number and electron density using an EMI scanner. *Neuroradiology, 1*, 15–21.

SPELLER, R. D. and WHITE, D. R., 1977. Determination of the effective keV in computerised tomography. (Poster Session) 14th International Congress of Radiology. Rio de Janeiro, 19–26 October.

STORM, E. and ISRAEL, H. I., 1970. Photon cross sections from 1 keV to 100 MeV for elements Z=1 to Z=100. *Nuclear Data Tables, A7*, 565–681.

WHITE, D. R. and FITZGERALD, M., 1977. Calculated attenuation and energy absorption coefficients for ICRP Reference Man (1975) organs and tissues. *Health Physics, 33*, 73–81.

WHITE, D. R., MARTIN, R. J., and DARLISON, R., 1977. Epoxy resin based tissue substitutes. *British Journal of Radiology, 50*, 814–821.

1980, *British Journal of Radiology, 53*, 12–20

The isocentric fast neutron therapy facility at Edinburgh

By D. E. Bonnett, Ph.D., M.Sc.,* J. R. Williams, M.Sc.† and C. J. Parnell, Ph.D., M.Inst.P.‡

*M.R.C. Cyclotron Unit, †Department of Medical Physics and Medical Engineering, Western General Hospital, Edinburgh and ‡M.R.C. Cyclotron Unit, Hammersmith Hospital, London

(*Received May 1979*)

ABSTRACT

A second fast neutron beam for radiotherapy has been brought into operation at the Western General Hospital, Edinburgh. This beam is isocentrically mounted and can be rotated through ±120 deg from the vertical. Neutrons are produced by bombarding a thick beryllium target with 15 MeV deuterons. The provision of an isocentric facility enables some of the problems associated with poor beam penetration to be alleviated. The physical features of the isocentric facility are described with particular reference to the shielding and the methods employed to overcome problems of neutron activation. Both the prompt radiation leakage and the induced activity have been measured. It has been found that for the first eight months of operation the whole body dose-equivalent to radiographers was approximately 6 μSv (0.6 mrem) per patient treated. Dosimetry associated with the facility is discussed and an example of a seven field treatment plan for a bladder is presented.

Both the cyclotron and the fixed horizontal neutron beam at the Western General Hospital, Edinburgh, have been discussed in a previous paper (Williams *et al.*, 1979). Recently a second beam has been brought into operation which is steerable and isocentric. As far as treatment planning is concerned the neutron dose distributions from the two beams are the same. However, the isocentric beam can be used to treat deep-seated tumours using multiple beam techniques not possible with the fixed horizontal beam.

This paper describes the isocentric unit and the studies carried out before the commencement of radiotherapy in May 1978, with particular reference to the special radiation protection problems encountered and the modifications to the machine which were found to be necessary.

ISOCENTRIC UNIT

General description

The isocentric unit, Fig. 1, consists of a gantry on which is mounted the deuteron beam transport system, beryllium target assembly, shielding and collimation system and the counter-balance. The gantry can be rotated through ±120 deg from the vertical and can be used for isocentric treatment techniques with a target–axis distance of 125 cm.

Following extraction from the cyclotron and selection of beam path by the switching magnet in the cyclotron vault, the deuteron beam enters the 45 deg bending magnet of the isocentric unit, passes through a singlet quadrupole magnet used for beam steering, and is finally bent through 135 deg before striking the beryllium target. The position of the beam on the target is monitored by a gold-plated circular iris consisting of four insulated quadrants, from each of which the current can be monitored separately. A similar iris system has been added at the entrance of the 135 deg magnet to minimize the possibility of the deuteron beam striking either the vacuum box or the poles of the magnet.

Neutrons are produced in a thick beryllium target (155 mg cm^{-2}) and are then monitored using a transmission ionization chamber mounted immediately beyond the target. A cross sectional diagram of this chamber is shown in Fig. 2. The three high voltage electrodes are connected in series, with the upper electrode connected to the high voltage supply. The voltage at the lower electrode is monitored and must be detected by the cyclotron control system before the deuteron beam can be directed into the isocentric unit. The two collecting electrodes, each of which collects ionization from the two air-filled cavities adjacent to it, are each connected to an independent dose-monitoring system identical to those used with the fixed horizontal beam.

The neutron shielding around the target and the collimators are constructed from Benelex, a high density (1.39 g cm^{-3}) compressed wood material produced by the Masonite Corporation. The collimators are interchangeable with those used on the fixed horizontal beam (Williams *et al.*, 1979), but with the isocentric unit a bayonet locking system is necessary to retain them in position. Wedges for the isocentric unit are made from high density polythene (0.95 g cm^{-3}) to give nominal wedge angles of 25, 35 and 45 deg. The holders for these wedges have been designed to give additional security to the bayonet locking system which holds the collimators in position.

Shielding

Figure 3 shows the profiles of the absorbed dose in tissue for neutrons and gamma radiation, expressed as a percentage of the total dose at the isocentre for an 11 cm × 11 cm field, and measured with the collimator aperture filled with a solid Benelex plug. Measurements were made along the axis of rotation

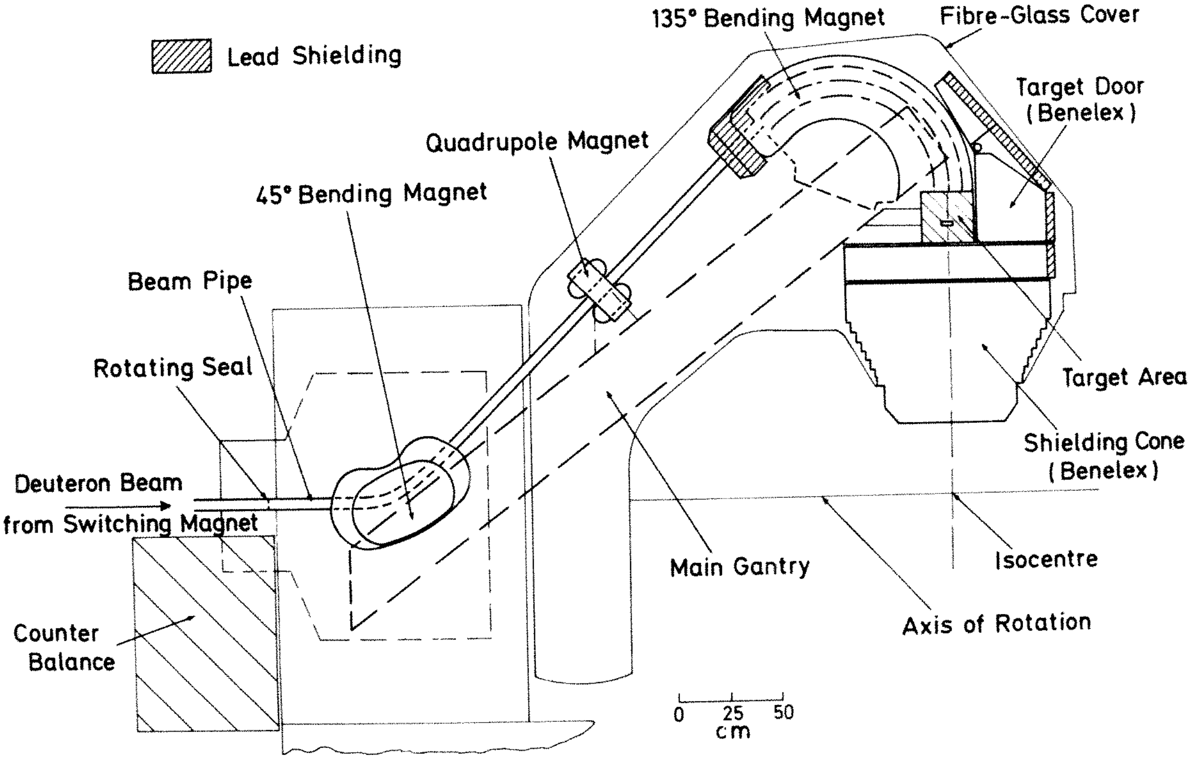


FIG. 1.
The isocentric beam transport system.

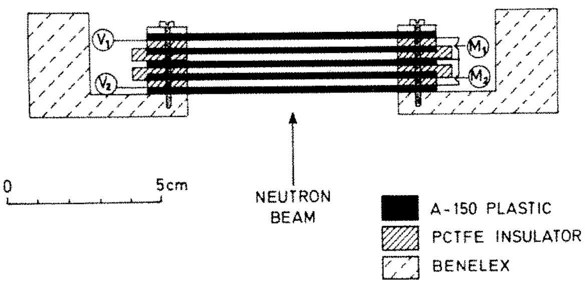


FIG. 2.
Cross sectional diagram of the monitor chamber. V_1 connection to the high voltage supply; V_2 connection to the high voltage detection system; M_1 and M_2 connections to the two neutron monitor systems.

of the unit to cover the range of positions at which any part of the patient could be positioned.

The two components of the absorbed dose in tissue were derived from measurements made with two detectors, a 0.5 cm^3 tissue-equivalent ionization chamber (Exradin, Inc.) which has a neutron sensitivity relative to its photon sensitivity (k_t) of 0.978, and a Geiger-Müller counter (Mullard type MX163) mounted in an energy-compensating shield and surrounded with lithium-6 to reduce its response to thermal neutrons. The neutron sensitivity of such a counter assembly relative to its photon sensitivity (k_u) has been estimated to be 0.007 for a similar neutron spectrum (Hough, 1979).

It can be seen from Fig. 3 that, with the exception of the region closest to the gantry, the neutron leakage dose is approximately constant at 0.3% of the total absorbed dose at the isocentre. This constancy arises because the thickness of the shielding material and the neutron production both decrease with angle from the central axis. The slight increase in neutron dose in the region closest to the gantry is attributed to a small fraction of the deuteron beam striking components of the rotating seal and the 45 deg bending magnet. The photon absorbed dose, although less than 0.5% of the total absorbed dose at the isocentre, shows greater variations than the neutron absorbed dose, with the minima in the gamma profile corresponding to the maximum radial lengths of shielding material in front of the target.

Although the total radiation leakage is greater than that permitted for X or gamma radiation machines, Bewley and Page (1978) have shown that the greatest proportion of the risk of a new malignancy resulting from neutron radiotherapy results from radiation

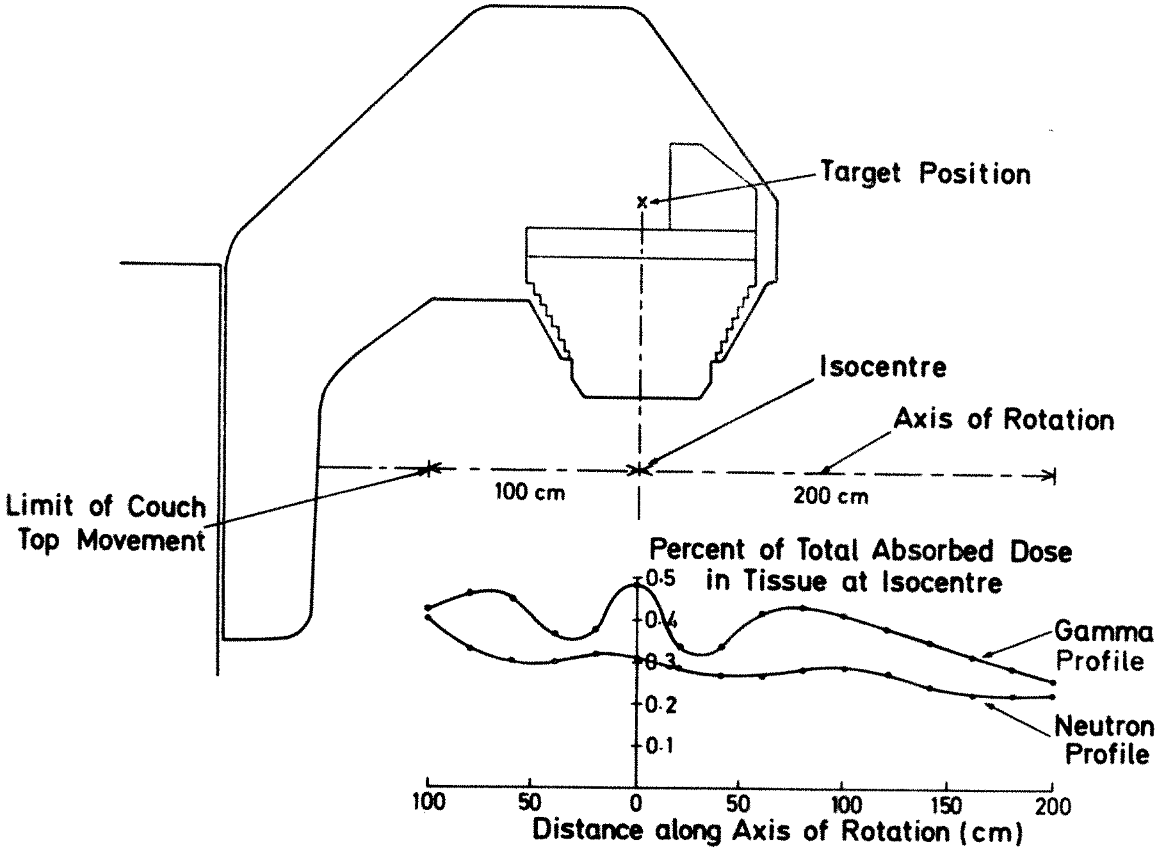


FIG. 3.

Profiles of neutron and γ-ray absorbed dose in tissue at the isocentre with the collimator aperture filled with a solid Benelex plug. Both profiles are normalized to 100% total absorbed dose at the isocentre for an 11 × 11 cm field.

TABLE I

ABSORBED DOSE-RATES IN WATER RESULTING FROM INDUCED ACTIVITY 20 CM FROM THE SURFACE, 5 MIN AFTER THE END OF IRRADIATION

Position†	Dose-rates (μGy/h) following shielding modification					Reduction factor*
	Original	Stage (a)	Stage (b)	Stage (c)	Stage (d)	
0	120	120	77	77	36	3.3
1	1120	270	170	100	70	16
2	4220	1100	330	200	46	92
3	500	180	130	83	82	6.0
4	270	88	82	66	52	5.2
5	80	80	62	61	38	2.1
6	780	490	360	220	218	3.6

*Reduction factor = original dose-rate/stage (d) dose-rate.
†The positions are shown on Fig. 5. For the four stages see text.

scattered from the primary beam within the patient and that the use of perfect collimation would only reduce the risk by 25%.

INDUCED RADIOACTIVITY

In external-beam neutron radiotherapy there are two potential radiation hazards to staff. The first, common to both neutron and photon radiation therapy, is the possibility of accidental exposure to the radiation beam due to failure of safety equipment or neglect of safety procedures. The second hazard, which is not encountered in photon therapy, is due

TABLE II

DOSE-RATES RESULTING FROM INDUCED ACTIVITY MEASURED ON THE SURFACE 2 MIN AFTER THE END OF IRRADIATION

Position	Dose-rate (μGy/h)		Reduction factor*
	Original	Stage (d)	
0	300	83	3.6
1	3540	250	14
2	13900	115	121
4	620	190	3.3
5	230	90	2.6

*Reduction factor = original dose-rate/stage (d) dose-rate.

to activation of materials which are irradiated with neutrons.

Before therapy commenced using the isocentric unit, measurements of absorbed dose-rates resulting from radioactivity induced in the unit were undertaken to assess the areas of potential hazard to staff. These measurements showed unacceptably high dose-rates initially (see for example Tables I and II) and modifications were carried out to the unit in an attempt to reduce the induced radioactivity to an acceptable level. The levels achieved have been discussed by Bonnett and Williams (1979). In this section the modifications made and the reductions in dose-rates achieved are discussed in greater detail.

The preliminary investigations indicated that the major cause of the observed radiation levels was activation of materials close to the beryllium target, and an analysis of the decay of the activity indicated that the principal components could be attributed to activation products from neutron interactions with aluminium. In particular, the principal component decayed with a half-life consistent with that of ^{28}Al (2.3 min), produced by the reaction ^{27}Al(n, γ)^{28}Al. This reaction has a cross section of 0.23×10^{-24} cm^2 at thermal neutron energies, the production of thermal neutrons being attributed to multiple scattering of the fast neutrons in the Benelex forming the shielding cone. In addition, two significant fast neutron reactions occur with aluminium, ^{27}Al(n,p)^{27}Mg and ^{27}Al(n,α)^{24}Na with product half-lives of 9.5 min and 15 hours respectively. All of the product nuclei from activation of aluminium decay with the emission of penetrating gamma radiation, the principal energies being 1.78 MeV (^{28}Al), 0.84 MeV and 1.01 MeV (^{27}Mg) and 1.37 and 2.75 MeV (^{24}Na).

To reduce the levels of induced radioactivity in the isocentric unit, three methods were used.

1. The installation of materials with a large thermal-neutron capture cross-section around the target assembly to capture thermal neutrons emanating from the Benelex. Initially gadolinium, in the form of gadolinium oxide, was considered because of its exceptionally large capture cross-section (46×10^{-21} cm^2) but was rejected because the associated production of prompt gamma radiation was found to be unacceptable. Instead, boron loaded rubber was used. Boron has a smaller capture cross section (0.77×10^{-21} cm^2) but has the advantage that the average number of photons produced per capture is smaller, 0.9 compared with 3.9 for gadolinium.

2. Materials with large activation cross-sections at thermal or fast neutron energies (*e.g.* aluminium) were replaced. Three alternatives, steel, pure iron (low manganese content) and titanium were considered, although the first two could not be used in close proximity to the 135 deg bending magnet because of their magnetic properties. In each of these materials the most abundant stable isotope has the largest thermal-neutron capture cross-section, but in each case the product formed is itself stable. In particular titanium has five stable isotopes, the heaviest of which (^{50}Ti) is only 5.3% abundant and has a thermal-neutron cross section of 0.179×10^{-24} cm^2, which is less than that of aluminium. The product of the reaction (^{51}Ti) decays with a half-life of 5.8 min with the principal gamma radiation having an energy of 0.32 MeV.

Initial tests with each material were carried out by observing the absorbed dose-rate in water from samples after irradiation in a paraffin wax block which increased the thermal-neutron component of the beam. From an analysis of the decay curves, absorbed dose-rates which would result following a series of irradiations were calculated assuming each irradiation to be of two minutes duration followed by an interval of 13 minutes. The results of these calculations together with those for aluminium sheathed in cadmium during irradiation are shown in Fig. 4. In the latter case cadmium was used to absorb thermal neutrons so that the resultant activity was due primarily to fast and epithermal neutrons and this was taken as an indication of the best that could be achieved without replacing any of the aluminium in the isocentric unit. It can be seen from Fig. 4 that, on the basis of equal volumes, titanium is the material of choice when more than three irradiations are carried out.

3. Additional shielding material was installed and some modifications to the existing shielding were made. Behind the target, additional Benelex was added to improve the neutron shielding and lead was added in selected positions to attenuate gamma radiation emitted from the areas of highest induced

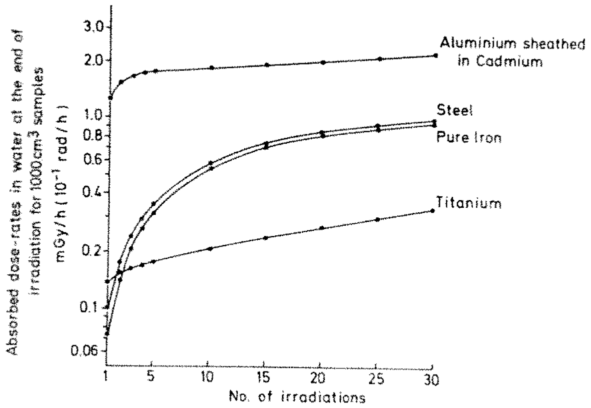


FIG. 4.

A comparison of the calculated build-up of absorbed dose in water due to induced activity in steel, pure iron, titanium and aluminium sheathed in cadmium.

activity. In addition, because of its close proximity to the target, the lead radiation shutter, provided to attenuate the gamma radiation from induced activity in and around the target emitted via the collimator aperture, was replaced with a shutter made of bismuth, since activation of bismuth would produce less gamma radiation than lead or any impurities contained in lead such as antimony.

These modifications were implemented in four stages and the positions of the changes are shown in Fig. 5. These four stages were:

(a) Lead shielding was added behind the target and at the entrance to the 135 deg bending magnet. In addition, thermal–neutron absorbing material, gadolinium oxide, was installed around the target area.

(b) Aluminium components in the target shielding

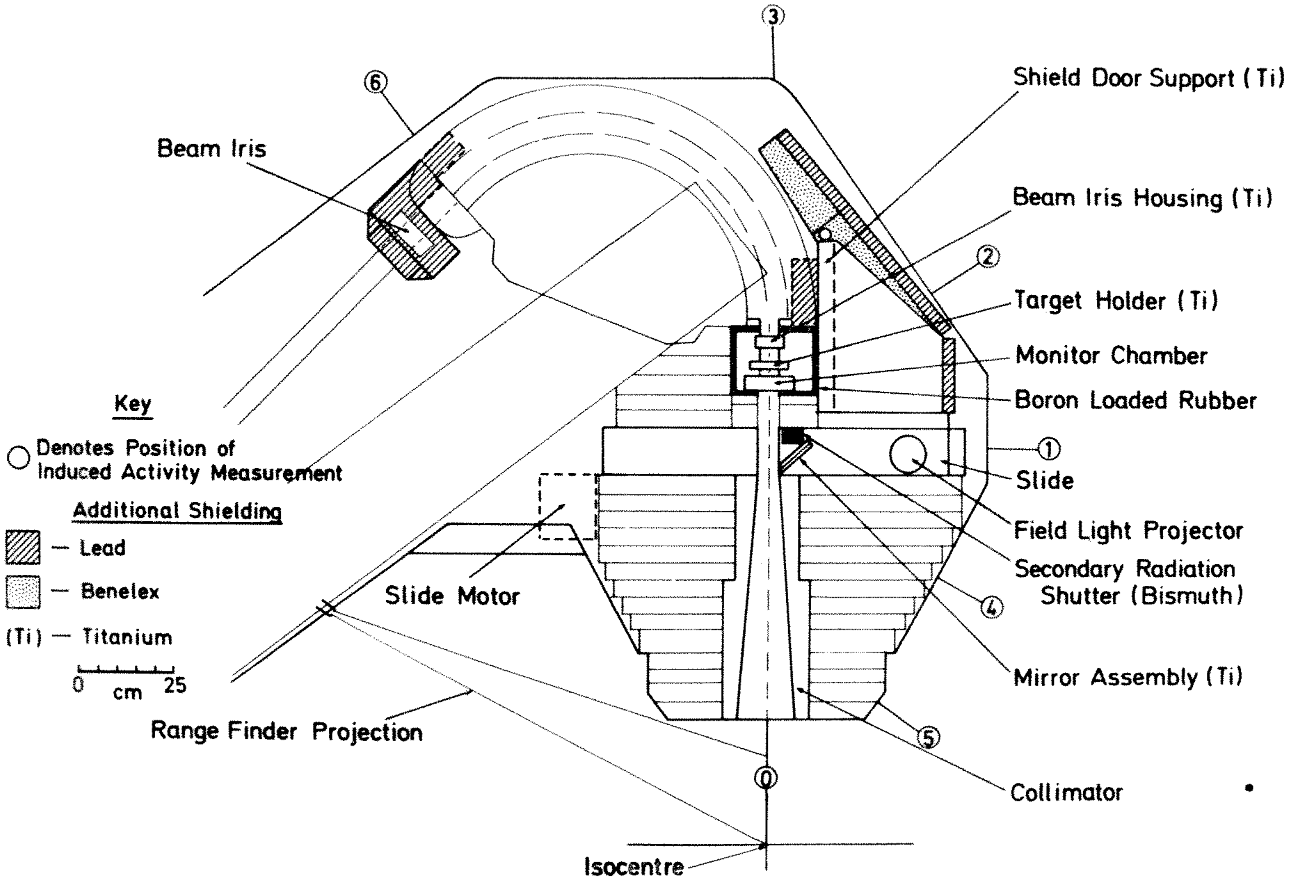


FIG. 5.

Location of changes in the isocentric shielding together with the position of the measurement of absorbed dose-rate due to induced activity.

door were replaced with components manufactured from titanium.

(c) Aluminium components in the target assembly, monitor chamber and beam-defining iris were replaced with titanium, and borated rubber was substituted for gadolinium oxide as a thermal–neutron absorbing material.

(d) Aluminium in the mirror assembly was replaced with titanium and the lead secondary radiation shutter was reconstructed from bismuth. Also, additional Benelex and lead shielding was added to the target shielding door and the rear of the target assembly.

Following each stage of modification, a beta-gamma dose-rate meter (NE 0500, Nuclear Enterprises Ltd.) was used to measure the absorbed dose-rates at various positions (labelled 0–6 in Fig. 5) both on and at 20 cm from the surface of the isocentric unit. However, it was not possible to make measurements under exactly the same conditions at each stage due to variations in the available deuteron beam current. In order to compare results each irradiation was of the same duration (three minutes) during which the beam current was kept constant and the results were corrected to give the levels of induced activity if a beam current of 100 μA had been used. This is equivalent to the delivery of approximately 1.3 Gy (130 rad) at the isocentre.

The results obtained following each stage of modification are shown in Table I, the distance of 20 cm and a time of five minutes from end of irradiation being parameters stated in the original specification. However, an initial high dose-rate due to short lived nuclides could present a hazard to staff entering the treatment room immediately after an irradiation. Consequently, Table II shows the results on the surface of the isocentric unit at one minute from the end of an irradiation.

Table I shows that the stage (a) modifications had the greatest overall effect, confirming the importance of minimizing activation by thermal neutrons. The replacement of aluminium and the addition of extra shielding also resulted in a significant reduction in absorbed dose-rate especially to positions 1 and 2 (Fig. 5). Position 5 shows the lowest overall reduction in dose-rate but it also had the lowest initial value indicating that, at that position, the dose-rate was only partially due to induced activity in and around the target assembly, the remainder being due to activation of the constituent materials of the Benelex shield. Activation of small samples of Benelex for one minute using the Hammersmith Cyclotron showed that the principal induced nuclides were ^{15}O ($T_{\frac{1}{2}}=2.0$ min) and ^{13}N ($T_{\frac{1}{2}}=10$ min), and analysis of the decay of annihilation gamma radiation indicated that, at the end of bombardment, the induced activity due to ^{15}O was approximately eleven times greater than that due to ^{13}N. In addition small quantities of ^{56}Mn and ^{24}Na were identified by gamma spectrometry and decay studies. Following prolonged irradiation by neutrons, gamma radiation attributed to ^{57}Co, ^{58}Co, ^{60}Co, ^{54}Mn, ^{65}Zn and ^{22}Na has been observed.

In addition to the production of short-lived nuclides following a single irradiation, the build-up of longer lived nuclides in the isocentric unit becomes of increasing importance during a typical radiotherapy session. Consequently, a radiotherapy session lasting four hours was simulated, assuming this to consist of an irradiation schedule of 1 Gy (100 rad) delivered in five minutes followed by a seven minute waiting period. During this seven minute interval the decay of the dose-rate at 20 cm from the surface of the isocentric unit was measured and the values at five minutes from the end of the irradiation were determined. For these measurements the two positions (3 and 6) at the rear of the unit were omitted and an additional position (7) located beside position 2 and directly over the target area was included. These results are shown in Fig. 6 and, in general, indicate that the build-up of activity, whilst not constituting a major hazard to staff, could with advantage be reduced. In particular the results from position 7 indicate a need for additional shielding in this region, but it should be noted that this area, and the corresponding position on the other side of the

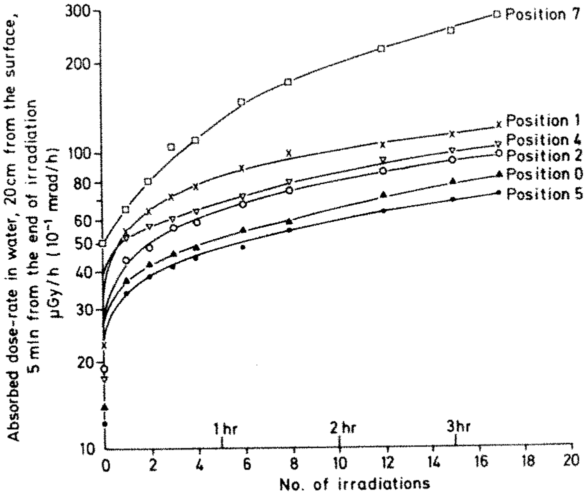


FIG. 6.

Measurements of the absorbed dose-rate in water due to build-up of induced activity around the isocentric unit.

unit, are usually remote from staff working in the treatment room.

From these measurements and a series of simulated treatments it was deduced that radiography staff would receive whole body dose-equivalents of approximately 8–12 μSv (0.8–1.2 mrem) per treatment, provided a waiting period of one minute after each irradiation was allowed, and that this would allow a radiotherapy programme to commence with a limited number of patients per day.

Following the commencement of radiotherapy the build-up of long lived nuclides ($T_{\frac{1}{2}} > 1$ day) was recorded. At the beginning of each week, the residual dose-rates were measured at the seven fixed points around the unit (Fig. 5) and the results for the first six months are shown in Fig. 7. Omitted from Fig. 7 are values obtained at positions 0 and 4 which were similar to position 5, and position 7 which was similar to position 2. The dose-rates shown in Fig. 7 depend upon the beam running time during the previous week but are small compared with the build-up over a four hour period (Fig. 6).

WHOLE BODY DOSES RECEIVED BY STAFF

During the first eight months of radiotherapy with the isocentric unit two radiographers worked together and each carried an extra beta-gamma film badge supplied and processed by the National Radiological Protection Board. These film badges were changed every four weeks and were carried only whilst working with the unit. The variation in the average of the two badge results in terms of dose-equivalent per treatment, together with the number of treatments, are shown in Fig. 8. The fifth four-week period represents abnormal operating conditions since it included a one-week cyclotron maintenance period when no treatments were undertaken. If this is excluded the mean dose-equivalent received by radiography staff per treatment during the eight month period was 5 μSv (0.5 mrem), whilst the inclusion of this fifth period increases the mean to 6 μSv (0.6 mrem). It should be noted that the radiographers wait one minute after the end of each treatment before entering the treatment room.

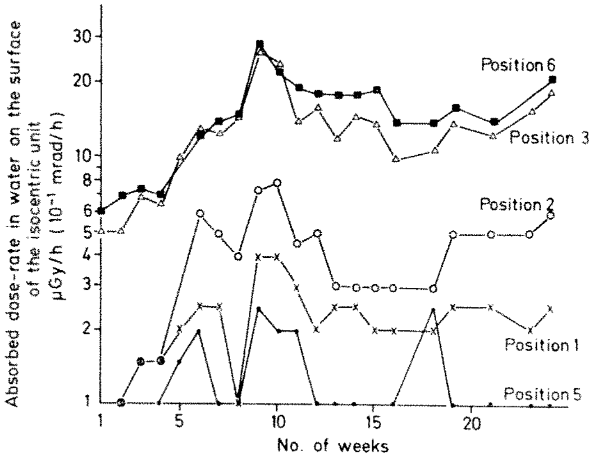


FIG. 7.

Residual dose-rates around the isocentric unit, at the beginning of each week during the first six months of treatment of patients.

It can be seen from Fig. 8 that, during this eight month period, the dose-equivalent received by the radiographers per treatment was not constant. This reflects variations in the complexity of the set-ups, the number of fields per patient, the efficiency and working habits of individual radiographers and the lack of precision in the film-badge results.

DOSIMETRY

On both the fixed horizontal beam and the isocentric unit, neutrons are produced by bombarding a thick beryllium target with 15 MeV deuterons. Thus, with the possible exception of small differences due to variations in shielding material and geometry between the two beams, the distributions of absorbed dose in tissue should be the same for the two beams. The techniques used for dosimetry and the measurement of isodose distributions have been discussed

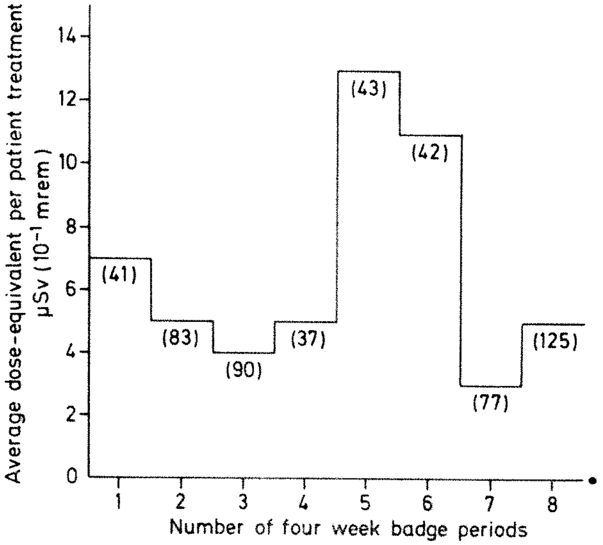


FIG. 8.

Variation in the average dose-equivalent per treatment received by radiographers during the first eight months of isocentric operation. The figures in brackets refer to the total number of patients treated.

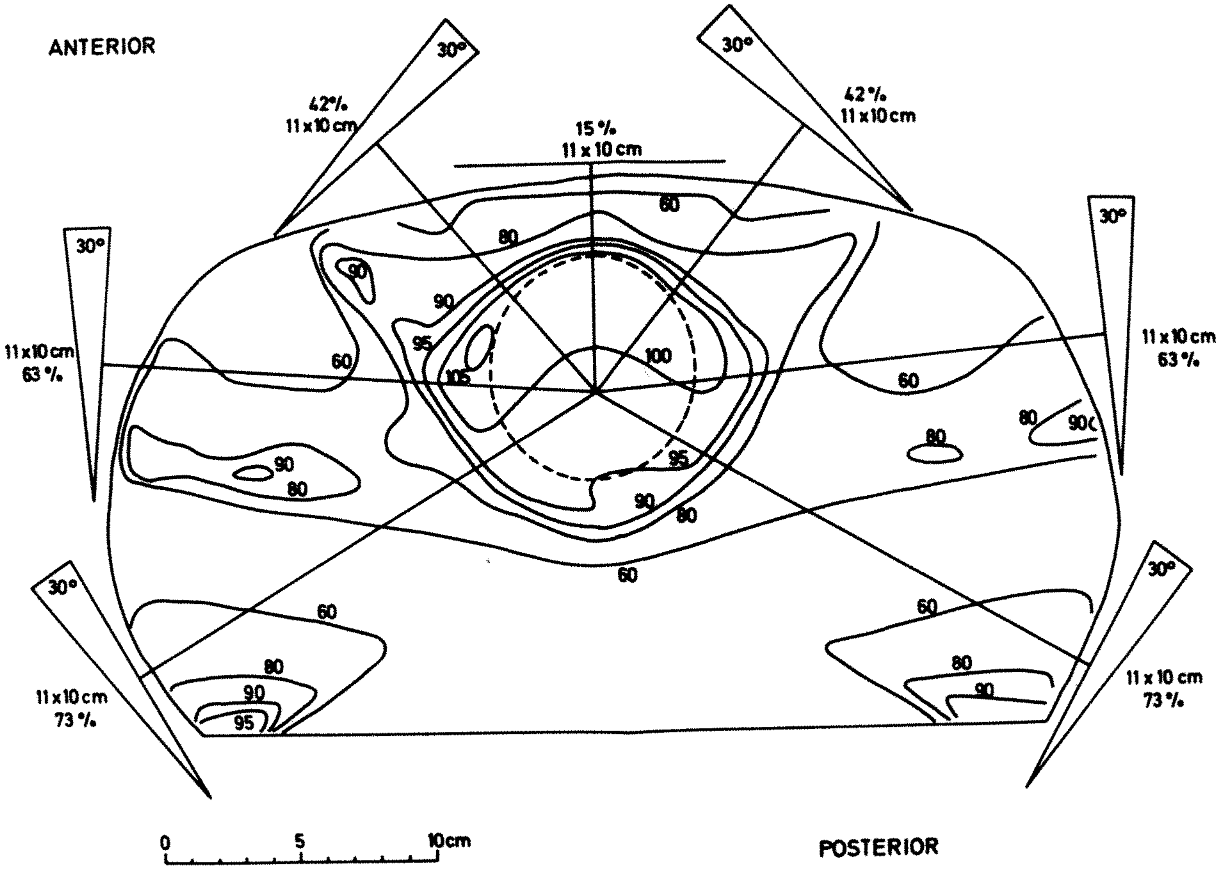


FIG. 9.
An example of a seven field treatment plan for the bladder.

previously (Williams *et al.*, 1979). Isodose curves measured with the isocentric unit showed no significant differences from those measured with the fixed horizontal beam and checks at three different angular positions of the unit indicated no dependence on angle.

The provision of the isocentric unit makes it possible to treat tumours in sites which could not be treated satisfactorily using a fixed horizontal beam. However, because of the poor beam penetration it is sometimes necessary to use up to seven fields to produce an acceptable dose distribution. An example of a treatment plan for the treatment of a bladder tumour using seven fields is shown in Fig. 9.

DISCUSSION

The isocentric unit at Edinburgh has been used for fast-neutron radiotherapy since May 1978. The inclusion of this isocentric facility has made it possible to treat deep-seated tumours such as those of the bladder, rectum and oesophagus, the treatment of which would have been impractical with a fixed horizontal or vertical beam. Poor beam penetration, however, has necessitated the use of up to seven treatment fields to produce an acceptable dose distribution. At a dose-rate of 0.25 Gy min^{-1} (25 rad min^{-1}) such treatments take approximately 15 minutes of beam time to deliver 0.80 Gy (80 rad) to the tumour volume per day. However, the use of a higher energy beam would simplify and improve such treatments.

If neutron radiotherapy is to be used more extensively it is important that future facilities should produce neutron beams with sufficient energy to provide depth doses comparable with modern X-ray units, and it is desirable that an isocentric unit should be incorporated in such a facility (Tran, 1978).

If the isocentric unit is to be used routinely for radiotherapy with the maximum throughput of patients, it is essential that the dose received by radiography staff should be well below current maximum permissible levels and should not produce any restrictions on their working methods. With the unit at Edinburgh it has been found that the average dose-equivalent to staff is approximately 6 μSv (0.6 mrem) per treatment. Potentially, the unit could be used to treat between 20 and 25 patients per day and this would result in a dose to a radiographer of between 120 and 150 μSv (12 and 15 mrem) per day which would be approximately two-thirds of the maximum permissible whole-body dose-equivalent.

Initial experiences at Edinburgh have shown the need for careful selection of materials to be used in an isocentric unit, especially those located close to the target. Such materials must have low activation cross-sections for both slow and fast neutrons and it is important that thermal-neutron absorbing materials be incorporated. In the design of a unit for use with higher energy neutrons, the lack of detailed knowledge of the behaviour of many important neutron cross-sections above 20 MeV indicates the need for experimental studies on both the activation and shielding properties of the materials under consideration. However, no matter how well the materials are chosen, some activity will be induced in the system and other methods of reducing the gamma radiation to an acceptable level, such as incorporating a lead shield on the outer surface, should be considered. Additionally, a "waiting period" can be used to allow levels of short-lived radionuclides to decay, but this not only causes additional inconvenience to patients but also limits the number of patients that can be treated.

ACKNOWLEDGMENTS

The completion of this project was made with the active co-operation of the Cyclotron Corporation and, in particular, we would like to acknowledge the help of Mr. J. L. Tom and Mr. G. O. Hendry.

We are also grateful to Mr. T. E. Saxton and the Cyclotron team for operating the machine, to Mr. W. M. Ranken for engineering assistance and to Mr. I. A. Masterton and Mr. I. D. Dudgeon for technical assistance.

REFERENCES

BEWLEY, D. K., and PAGE, B. C., 1978. On the nature and significance of the radiation outside the beam in neutron therapy. *British Journal of Radiology, 51*, 375–380.

BONNETT, D. E., and WILLIAMS, J. R., 1979. The isocentric fast neutron facility at Edinburgh. In *3rd Meeting on Fundamental and Practical Aspects of Fast Neutrons and other High LET Particles in Clinical Radiotherapy*—The Hague. To be published in the *European Journal of Cancer*.

HOUGH, J. H., 1979. A modified lead attenuation method to determine the fast neutron sensitivity k_u of a photon dosimeter. *Physics in Medicine and Biology, 24*, 734–747.

TRAN, D. T., 1978. Use of cyclotron produced neutrons for radiotherapy. In *Proceedings of the Third Symposium on Neutron Dosimetry in Biology and Medicine*, Neuherberg 1977. (EUR 5848). G. Burger, and H. G. Ebert, eds. (Commission of the European Communities) 347–356.

WILLIAMS, J. R., BONNETT, D. E., and PARNELL, C. J., 1979. The fixed horizontal neutron therapy beam at Edinburgh: dosimetry and radiation protection. *British Journal of Radiology, 52*, 197–208.

Book review

Newer Radiogases in Practice. Progress in Nuclear Medicine 5. Edited by M. Guter, pp.viii+244, 107 figs, 1978 (S. Karger, Basel—New York) $64.00.
ISBN 3-8055-2886-8

The use of "new" radioactive gases (^{15}O, ^{13}N, ^{81m}Kr, ^{127}Xe, ^{77}Kr) for both research and clinical diagnosis is one of the most exciting recent developments in nuclear medicine. As this topic has never been comprehensively covered before, a book on it was more than justified. This volume collects contributions from 13 authors, mainly from American institutions.

The section on lung ventilation scanning contains some interesting articles including two chapters on ^{127}Xe (good but very similar), two on ^{81m}Kr, one on ^{13}N, and an excellent paper on the relative advantages and disadvantages of gaseous and particulate tracers for ventilation scanning.

The rest of the book is not really worthwhile. In the section "Gas as a perfusion radioagent" will be found a rewriting of a technique recently published for obtaining multicolour images of cerebral perfusion with ^{133}Xe and carotid injection, a discussion on compartmental models for interpreting ^{133}Xe wash-out curves from the brain, and a brief (two pages) article entitled "Perfusion agents given by inhalation" where surprisingly no mention is made of most of the published work on the use of $^{15}O_{22}$, ^{77}Kr, and ^{81m}Kr for studies of regional blood flow and metabolism in the heart and brain. Some information on this would have probably been more appropriate (considering the title of the book) than the two last chapters "^{14}C Breath analysis" and "Radioiodine as a gas").

Altogether, the book is rather superficial and fails to take into account the considerable work done, in this field, outside the United States; a more comprehensive and at the same time more essential text remains yet to be written.

F. FAZIO.

1980, *British Journal of Radiology*, *53*, 21–25 JANUARY 1980

Late functional changes in the vasculature of the rat brain after local X-irradiation

By H. F. Moustafa, D.Phil. and J. W. Hopewell, Ph.D.

Churchill Hospital, Research Institute, University of Oxford

(*Received November 1978 and in revised form March 1979*)

ABSTRACT

The brains of young adult rats were irradiated with doses of 500–4000 rad. At intervals of 3–15 months after irradiation regional changes in the functional vasculature were investigated using the iodoantipyrine extraction technique. Modifications in vascular function were restricted to animals locally irradiated with doses of 2000 and 3000 rad. The first change was observed three months after irradiation and was characterized by a reduction in antipyrine extraction in the mid-brain and brain stem of animals irradiated with 2000 rad. At six and nine months after exposure to both 2000 and 3000 rad significant increases in antipyrine extraction were found in the four brain regions examined, although the effect was greatest in the mid-brain. These results are compared and contrasted with functional changes reported in other normal tissues; the link between these functional changes in the brain vasculature and the appearance of gross vascular lesions after a latent period of one year is discussed. It is suggested that the increase in iodoantipyrine extraction represents a regulatory reaction by the vasculature of the brain to tissue hypoxia and that focal vascular lesions in the brain occur as a consequence of the failure of this reaction to hypoxia.

In the treatment of some head and neck tumours by radiotherapy, late radiation-induced changes in the central nervous system occasionally present as an unacceptable complication (Gangloff and Hug, 1965). The mechanism responsible for the development of these late sequelae is not fully understood, although it is generally accepted that vascular effects are an important contributory factor (Duggar, *et al.*, 1954; Haymaker, 1962). In experimental and human post-mortem material vascular lesions are distributed throughout the grey and white matter of the central nervous system. These lesions are focal and are usually characterized by fibrinoid or hyaline changes in the walls of blood vessels (Berg and Lindgren, 1958; Hopewell and Wright, 1970). The reason for the somewhat random distribution of these focal lesions is unknown.

While the distribution of these gross pathological lesions may be random it seems reasonable to assume that they may be either preceded by or associated with more general disturbances in the functional vascularity of the central nervous system. Demonstration of this assumption is attempted in the present paper by the study of the time-related changes in the extraction of ^{125}I antipyrine (Sapirstein and Hanusek, 1958) in different regions of the rat brain after exposure to a range of single doses of X rays.

A previous histological study (Hopewell and Wright, 1970) in the rat brain suggested that death from vascular radiation damage was restricted to doses in the range 2000 to 3000 rad. With higher doses vascular effects were reduced and did not seem to be a contributory cause of death. The large areas of necrosis produced by these doses were restricted to white matter and would seem to result from the loss of neuroglial cells (Hopewell and Cavanagh, 1972; Hubbard and Hopewell, 1979). It was hoped that the present functional studies might provide additional evidence for, and an explanation of, the apparent loss of vascular effects with doses greater than 3000 rad.

MATERIALS AND METHODS

The brains of groups of young adult (12 week) female Sprague-Dawley rats were locally irradiated with single doses of 500, 1000, 2000, 3000 and 4000 rad of X rays, while the animals were under chloral hydrate anaesthesia (300 mg/kg). The irradiation was given laterally through the side of the head using 2.0 cm diameter semicircular apertures and parallel-opposed fields. Irradiation was given at 130 rad/min from 250 kV X-ray units operating at 15 mA with 0.5 mm Cu and 1.0 mm Al added filtration (HVL, 1.3 mm Cu). Groups of age matched animals acted as controls.

At intervals of 3, 6, 9, 12 and 15 months after irradiation, groups of four to six irradiated and age-matched control animals were used to examine regional changes in the cerebral circulation using the iodoantipyrine (^{125}I) extraction technique (Sapirstein and Hanusek, 1958).

The following standard procedure was followed: under chloral hydrate anaesthesia a femoral vein was exposed and a bolus of ^{125}I antipyrine injected (2 μCi in 0.1 ml). After an interval of 15 seconds the animal was killed by decapitation with a guillotine. The skull was then rapidly opened and the brain, without the olfactory lobes, dissected out. The brain was carefully subdivided into four parts, the cerebellum, brain stem, mid-brain and cerebral

---

Reprint requests to Dr. J. W. Hopewell.

P25843

hemispheres. Each part was placed into separate isotope counting vials; the volume of material in each vial was then made up to 2 ml by the addition of formol saline. The activity of ^{125}I in each sample was then measured using a well-type NaI detector connected to a multichannel analyser (Nokia 4840). The activity of ^{125}I in the whole brain was obtained by the summation of the radioactive counts for each brain region. The activity of standard dilutions of the injected tracer activity was evaluated at the same time.

The weight of each brain region was obtained after a standard fixation period of two weeks, and after their radioactivity had been counted. The total weight of each individual brain was obtained by simple addition. All extraction ratios were calculated relative to unit mass of fixed brain tissue.

RESULTS

In the six-month-old rat (three months after sham irradiation) approximately 2.6% of the injected iodoantipyrine tracer activity is extracted by the whole brain. Regional variations in the extraction of iodoantipyrine appeared to be related to the weights of the different brain regions, the extraction ratio per gram of tissue being the same in each part of the brain examined (Fig. 1). There was also little variation in extraction ratio with increasing age. For the whole brain the slight fall in extraction ratio with age only proved significant between the 12 and 15 month points ($p < 0.05$). There was no significant difference between individual groups in the 3 and 12 month points. The reasons for the high extraction ratios in the cerebellum and brain stem of the animals killed six months after sham irradiation could not be explained. This result can only be viewed as an artifact.

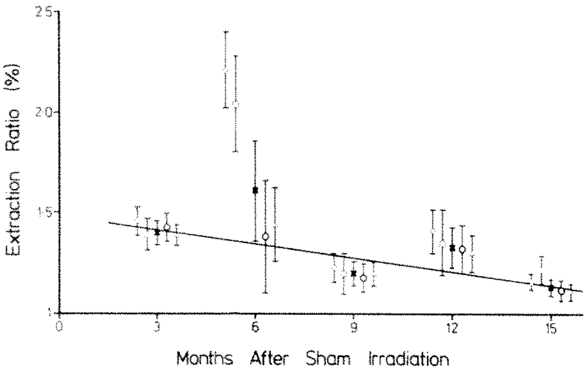


FIG. 1.

Changes in the extraction ratio of iodoantipyrine (^{125}I) per gram of tissue in the whole brain (×), mid-brain (○), cerebral hemispheres (△), cerebellum (□) and brain stem (◇) of unirradiated rats with time after sham irradiation. (Error bars are standard error of the mean.)

In the irradiated brains, changes in functional vascularity related to both time and dose were observed (Figs. 2 and 3). After a latent period of three months the relative extraction ratio for the whole brain was reduced after a dose of 2000 rad, although this did not reach accepted levels of significance ($p = 0.065$). This finding was reinforced by the significantly reduced extraction ratios in both the mid-brain and brain stem ($p < 0.05$). This reduction in extraction ratio was transient and by six months there was a suggestion of an increase in the extraction ratio in the whole brain after a dose of 2000 rad. Again the difference did not reach accepted levels of significance, although this may be due to the large standard error on the aged-matched controls. The increase in iodoantipyrine extraction was significantly increased ($p < 0.01$) in the mid-brain but not in the cerebral hemispheres. Changes in the cerebellum and brain stem could not be assessed because of the artifactually high extraction values obtained in the age-matched control animals.

An increase in antipyrine extraction was also found nine months after irradiation. Changes were limited to brains irradiated with doses of 2000 and 3000 rad. The rise was significant in all brain regions including the cerebral hemispheres. No significant regional variations could be established. No significant modification in antipyrine extraction was observed after doses of 500, 1000 or 4000 rad in any brain region at this time.

This increase in tracer extraction after irradiation with 2000 and 3000 rad was again a transient phenomenon and at 12 months after irradiation no modification in brain antipyrine could be demonstrated. In brains irradiated with doses in the range 500 to 2000 rad and examined 15 months after irradiation, the only modification in antipyrine extraction found was a small (15.9%) but significant rise in the cerebral hemispheres of brains exposed to 2000 rad (Fig. 3).

DISCUSSION

The iodoantipyrine technique is based on the principle that the early distribution of the tracer within organs and tissues is a measure of the distribution of the cardiac output, *i.e.* the regional blood flow (Sapirstein, 1958). The present study suggests that in the young adult rat approximately 2.6% of the cardiac output provides the circulation to the brain. This value is somewhat higher than the value of 1.64% originally obtained by Sapirstein and Hanusek (1958). The strain of rat and type of anaesthesia used in the present study were, however, different from those used by the previous authors.

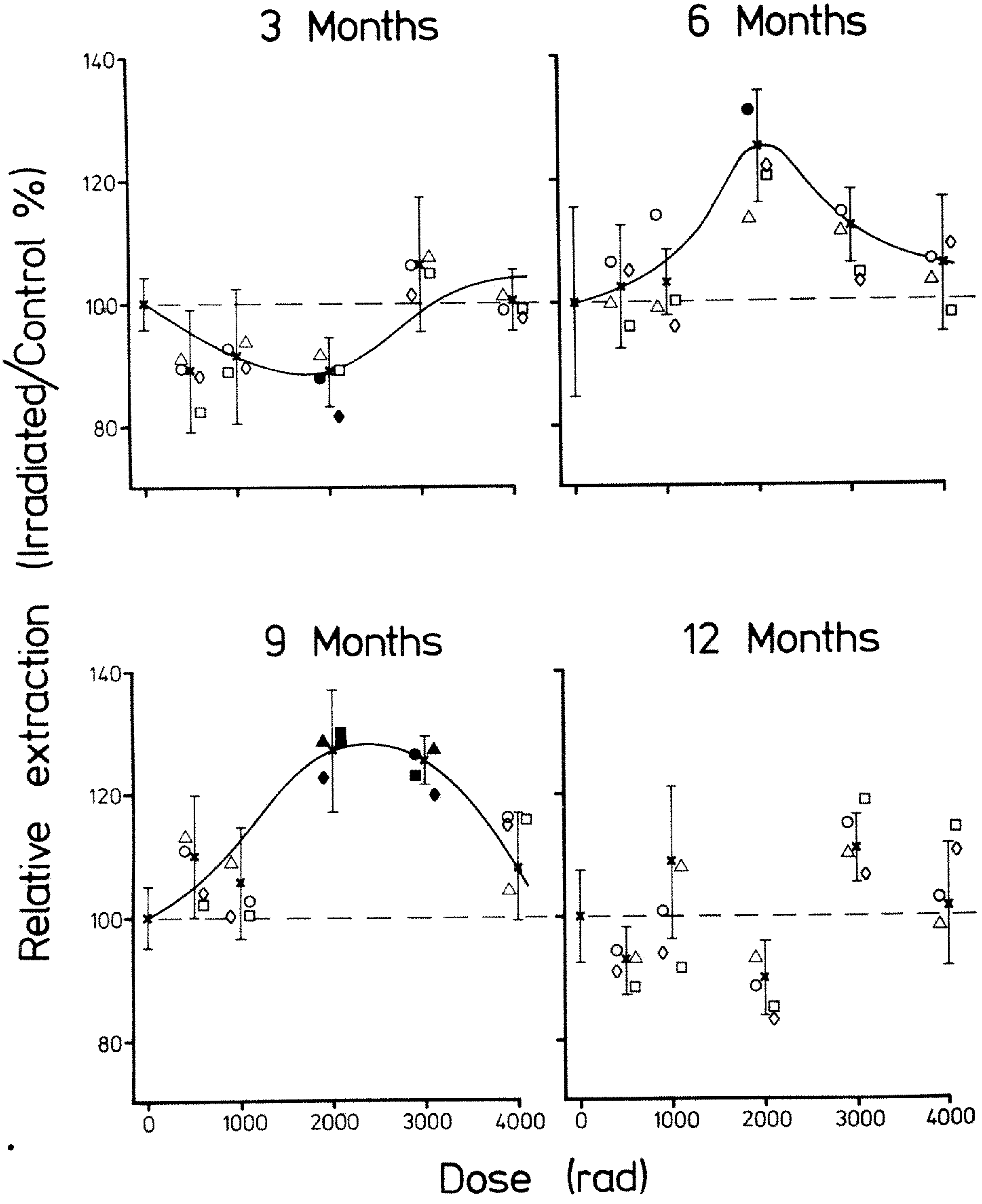


FIG. 2.

Dose-related changes in the relative extraction of iodoantipyrine (irradiated/control %) in the whole brain (±SE) and the four separate brain regions at periods of 3, 6, 9 and 12 months after irradiation. Key as in Figure 1. Significant changes in antipyrine extraction in the different brain regions are indicated by solid symbols.

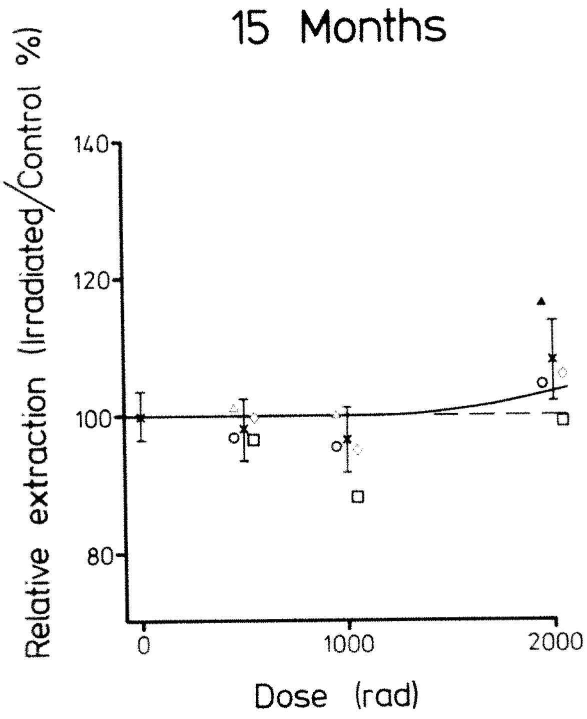


Fig. 3.

Dose-related changes in the relative extraction of iodoantipyrine (irradiated/control %) in the whole brain (±SE) and the four separate brain regions 15 months after irradiation. Key as in Figures 1 and 2.

Parameters of cephalic blood flow have been shown to be strain-dependent in rats (Keyeux, 1976). A reduction in cerebral blood flow with increasing age is also compatible with previously published results (Keyeux *et al.*, 1971; Keyeux, 1976).

In the irradiated brains, changes in iodoantipyrine extraction were found that could be related to both a decrease and an increase in cerebral blood flow. These changes were restricted to brains irradiated with doses of 2000 and 3000 rad. Previous histological studies have shown vascular damage to be important in the pathogenesis of late radiation damage in the rat brain at these dose levels (Hopewell and Wright, 1970). After exposure to a dose of 4000 rad no functional changes were observed in the mid-brain or cerebral hemispheres; this observation is again consistent with previous histological findings, as vascular lesions were not found to be important after exposure of the rat brain to this level of radiation dose. Comparable histological findings have also been reported in the irradiated spinal cord (Innes and Carsten, 1961; Hopewell and Wright, 1975; Hubbard and Hopewell, 1979). A reduction in vascular lesions when the irradiation dose was increased has also been reported in the kidney (Casarett, 1964) and skin (de Ruiter and van Putten, 1975) and possible explanations have been discussed in detail elsewhere (Hopewell, 1974; Hopewell and Young, 1978).

The links between the modifications in vascular function reported here and the appearance of gross vascular lesions observed one to two years after irradiation (Hopewell and Wright, 1970; Hopewell *et al.*, 1978a) are supported by regional variations found in iodoantipyrine extraction. In the mid-brain increased antipyrine extraction was observed at six months after irradiation with 2000 rad. This increase was found in the mid-brain and cerebral hemispheres nine months after irradiation with 2000 and 3000 rad. In histological material gross vascular lesions are most frequently reported in the mid-brain (Hopewell *et al.*, 1978b), the hypothalamus being particularly susceptible (Haymaker, 1962; Hopewell and Wright, 1970). The cerebral hemispheres on the other hand rarely show evidence of vascular damage (Hopewell *et al.*, 1978b).

While the above discussion supports the hypothesis that the reported functional modification both precede and result in the observed morphological changes, no comprehensive explanation is available. It is, however, possible to speculate on the likely mechanisms involved. The suggestion of a transient reduction in iodoantipyrine extraction three months after irradiation with a dose of 2000 rad is compatible with changes seen in other normal tissues three to six months after irradiation (Hopewell and Young, 1978; Hopewell *et al.*, 1978a; Glatstein, 1973; Nielson *et al.*, 1977). In some of these tissues the impairment in vascular function has been attributed, at least in part, to focal occlusive changes in arterioles (Hopewell and Young, 1978; Hopewell *et al.*, 1978a). It seems possible that a similar mechanism may be important here as occlusive vascular changes have already been reported at this time in the irradiated rat brain (Hopewell, 1974).

The hypoxia resulting from the impairment of vascular function in tissues such as pig skin and the hamster cheek pouch (Hopewell *et al.*, 1978a; Hopewell and Young, 1978) seems likely to be a cause of the subsequent tissue atrophy. In the brain, however, tissue hypoxia may result in an increase in blood flow and total cerebral blood volume. This is suggested by the similarities between the modifications of brain circulation with time after irradiation and the increase in cerebral blood flow in rats breathing increasing concentrations of carbon dioxide (Keyeux and Ochrymowicz-Bemelmans, 1978). The increase in antipyrine extraction found after six to nine months may thus represent a prolonged vasoregulatory response to tissue hypoxia. Other evidence of increased blood flow in brain as a late consequence of X-irradiation has been reported by Keyeux *et al.* (1971). These findings are consistent with recent quantitative histological studies (Hopewell *et al.*, 1978b) which have demonstrated a significant vasodilation and subsequent increase in vascular volume in the rat cerebral cortex nine months after irradiation with 2000 rad. The increase in iodoantipyrine extraction may simply be a reflection of the increased area of blood vessel wall available to the tracer, as opposed to a true increase in cerebral blood flow. Alternatively other factors may be involved; these might include an extension of the extravascular iodoantipyrine cerebral distribution space or an increase in the tissue/blood partition coefficient for the tracer, although both of these alternatives would be difficult to verify. The permeability coefficient for iodoantipyrine through the vessel wall may also be modified by irradiation. However, iodoantipyrine is believed to be a freely diffusible tracer across the walls of cerebral vessels and, although a reduction in permeability might be expected after irradiation, it is thought very unlikely that it would be increased and hence explain the present experimental findings.

While the final link between increased antipyrine extraction and focal vascular lesions is unclear, it is possible to speculate that the latter occur as a consequence of the random failure of the reaction of the cerebral vasculature to hypoxia. The excessive dilation of blood vessels may result in weakness of the vessels and the development of microaneurysms, thrombosis or haemorrhage. Dilation of vessels could in the long term produce the fibrinoid and hyaline changes often seen in the irradiated vessels of the brain (Hopewell and Wright, 1970). The greater oxygen requirement of the mid-brain as compared with the cerebral hemispheres would account for the more marked functional effects noted in the mid-brain and for the subsequent appearance of a greater number of vascular lesions in this region.

ACKNOWLEDGMENTS

The authors are indebted to Messrs. F. Dickinson and P. Thompson for their care of the animals and to Mrs. E. Whitehouse and Mr. J. Wilkinson for technical assistance. One of us (H.F.M.) wishes to acknowledge financial support from the Egyptian Ministry of Higher Education during his D.Phil. studies, of which the work presented here forms a part. This work was also carried out as part of a collaborative research programme of the European Late Effects Project Group (EULEP).

The Churchill Hospital Research Institute is supported by a grant from the Cancer Research Campaign.

REFERENCES

BERG, N. O. and LINDGREN, M., 1958. Time dose relationship and morphology of delayed radiation lesions in the brain of rabbit. *Acta Radiologica, Supplement, 167*, 1–118.

CASARETT, G. W., 1964. Pathology of single intravenous doses of polonium. *Radiation Research, Supplement, 5*, 246–321.

DUGGAR, G. S., STRATFORD, J. G. and BOUCHARD, J., 1954. Necrosis of the brain following Roentgen irradiation. *American Journal of Roentgenology, 72*, 953–959.

GANGLOFF, H. and HUG, O., 1965. The effects of ionizing radiation on the nervous system. *Advances in Biology, Medicine and Physics, 10*, 1–90.

GLATSTEIN, E., 1973. Alterations in rubidium-86 extraction in normal tissues after irradiation. An estimate of long-term blood flow changes in kidney, lung, liver, skin and muscle. *Radiation Research, 53*, 88–101.

HAYMAKER, W., 1962. Morphological changes in the nervous system following exposure to ionizing radiation. In: *Effects of Ionizing Radiation on the Nervous System*—IAEA, Vienna, pp. 309–358.

HOPEWELL, J. W., 1974. The late vascular effects of radiation. *British Journal of Radiology, 47*, 157–158.

HOPEWELL, J. W. and CAVANAGH, J. B., 1972. Effects of X-irradiation on the mitotic activity of the subependymal plate of rats. *British Journal of Radiology, 45*, 461–465.

HOPEWELL, J. W., FOSTER, J. L., GUNN, Y., MOUSTAFA, H. F., PATTERSON, T. J. S., WIERNIK, G. and YOUNG, C. M. A., 1978a. Role of vascular damage in the development of late radiation effects in pig skin. In: *Late Biological Effects of Ionizing Radiation*—IAEA, Vienna, *1*, 483–492.

HOPEWELL, J. W., REINHOLD, H. S., WILKINSON, J. and BLACKIEWICZ, B., 1978b. Changes in the architecture of blood vessels in the rat brain after local irradiation. *British Journal of Radiology, 51*, 561.

HOPEWELL, J. W. and WRIGHT, E. A., 1970. The nature of latent cerebral irradiation damage and its modification by hypertension. *British Journal of Radiology, 43*, 161–167.

HOPEWELL, J. W. and WRIGHT, E. A., 1975. The effects of dose and field size on late radiation damage in the rat spinal cord. *International Journal of Radiation Biology, 28*, 325–333.

HOPEWELL, J. W. and YOUNG, C. M. A., 1978. Changes in the microcirculation of normal tissues after irradiation. *International Journal of Radiation Oncology, Biology and Physics, 4*, 53–58.

HUBBARD, B. M. and HOPEWELL, J. W., 1979. Changes in the neuroglial cell population of the rat spinal cord after local X-irradiation. *British Journal of Radiology, 52*, 816–821.

INNES, J. R. M. and CARSTEN, A., 1961. Demyelination or malacic myelopathy. *Archives of Neurology, 4*, 190–199.

KEYEUX, A., 1976. Late modifications of cephalic circulation in head X-irradiated rats. *Radiation and Environmental Biophysics, 13*, 125–135.

KEYEUX, A., DUNJIC, A., ROYER, E., JAVANOVIC, D. and VAN DER MERCKT, J., 1971. Late functional and circulatory changes in rats after local irradiation. *International Journal of Radiation Biology, 20*, 7–25.

KEYEUX, A. and OCHRYMOWICZ-BEMELMANS, D., 1978. Late response of the cerebral circulation to X-irradiation of the brain in the rat. In: *Late Biological Effects of Ionizing Radiation*—IAEA, Vienna, *2*, 251–260.

NIELSON, D. F., CHAFFEY, J. T. and HELLMAN, S., 1977. Late effects of X-irradiation on the ability of mouse bone marrow to support haematopoiesis. *International Journal of Radiation Oncology, Biology and Physics, 2*, 39–45.

DE RUITER, J. and VAN PUTTEN, L. M., 1975. Measurement of blood flow in the mouse tail after irradiation. *Radiation Research, 61*, 627–638.

SAPIRSTEIN, L. A., 1958. Regional blood flow by fractional distribution of indicators. *American Journal of Physiology, 193*, 171–168.

SAPIRSTEIN, L. A. and HANUSEK, G. E., 1958. Cerebral blood flow in the rat. *American Journal of Physiology, 193*, 272–274.

1980, *British Journal of Radiology*, *53*, 26–28

Technical notes

Target angle and inferential kilovoltage measurement

By H. E. Crooks, F.C.R.

Environmental and Medical Sciences Division, AERE, Harwell, Oxon

(Received December 1978 and in revised form April 1979)

When checking kilovoltage inferentially, such as when using the penetrameter described by Ardran and Crooks in 1967 and 1968, fairly heavy added filtration is used in order to obtain X-ray beam homogeneity and also to reduce or eliminate the effect of target angle, extra focal radiation, target roughening and pitting and spurious X rays. This is effective when X-ray targets are not badly pitted and when target angles vary by only a few degrees from that used for calibration. This point was recognized in 1965 during testing of the penetrameter and discussed by Ardran and Crooks (1967). If, however, the target angle to be measured is widely different from that used for calibration (especially when one anode is very steeply angled) the difference in X-ray quality due to target filtration could be translated into a change in effective kilovoltage of several kV in the high kilovoltage range.

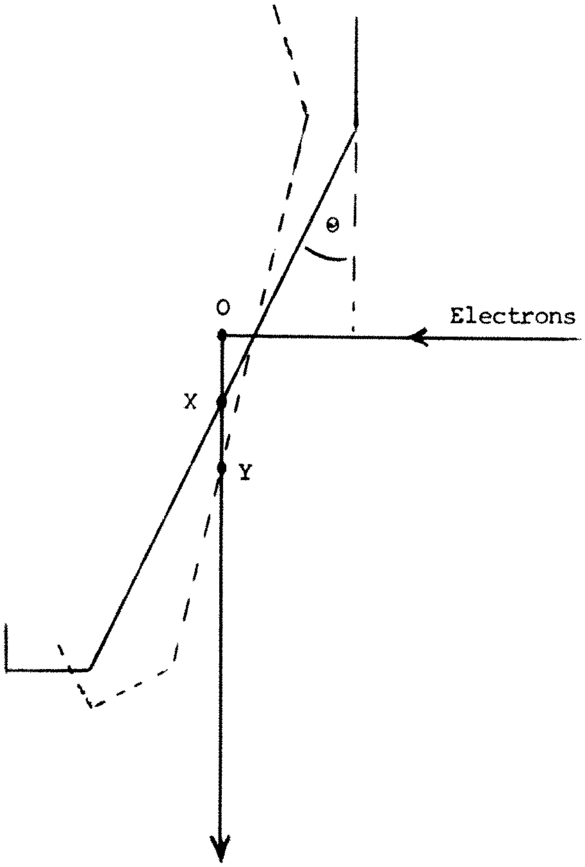


FIG. 1.
The effect of target angle on the path length through the target material of X rays generated at 0.

The effect of target angle is illustrated in Fig. 1. For X rays generated at a point within the target, such as O, decreasing the target angle θ as shown by the dotted line in Fig. 1 increases the path length through the target material from OX to OY, and hence because of the additional filtration increases the effective kV. Zintheo (1937) has shown that X-ray quality varies with angle of emergence from the anode, and that increasing filtration of the primary beam reduces but does not eliminate the variation. Ardran and Crooks (1972) observed that this change of quality could introduce errors in inferential estimation of inherent tube filtration and produced correction data.

Figure 2 and Table I give details of the effective variation to be expected in the diagnostic range. These figures were obtained by rotating one 10 deg and three 17 deg target-angle tubes about an axis perpendicular to the anode-cathode axis and parallel to the plane of the penetrameter in order to give a range of effective target angles. Thus when a 17 deg target tube is rotated 7 deg in the anode direction, the effective angle becomes 24 deg, while if a 10 deg target tube is rotated 6 deg in the cathode direction the effective target angle becomes 4 deg. It is appreciated that the angle of incidence of the electron beam also alters during these manoeuvres; evidence using the 10/17 deg target angles Siemens Biangulix tubes with similar direction electron beams suggests that changing the electron-beam angle does not, in this context, significantly alter the radiation quality expressed in Fig. 2, while Birch (private communication) has confirmed that there is close agreement between these figures and theoretical spectrometric values.

During the experiments the light-beam diaphragm, the maker's initial beam limiting collar and our own extra-focal radiation-limiting "bung" were

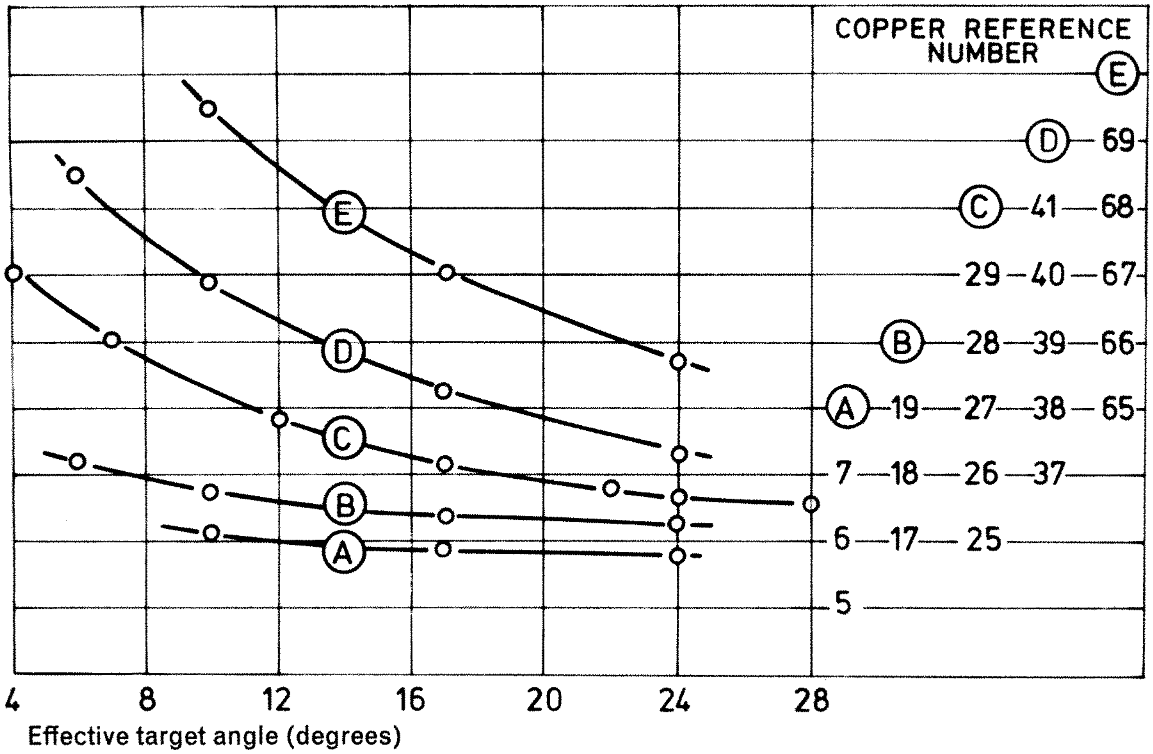


FIG. 2.

A. 40 kV (nominal) 0.6 mm Cu added filtration
B. 60 kV (nominal) 1.5 mm Cu added filtration
C. 80 kV (nominal) added filtration
D. 96 kV (nominal) added filtration
E. 148 kV (nominal) added filtration

Inherent filtration was standardized for all tubes at 1.0 mm Al by adding suitable amounts of aluminium. The scale on the ordinate is different for each curve and is shown on the right-hand side.

TABLE I

Target angle (degrees)	Nominal kilovoltage									
	40*		60*		80†‡		96†		148‡	
	CRN	Effective kVp§	CRN	Effective kVp	CRN	Effective kVp	CRN	Effective kVp	CRN	Effective kVp
10	6.1	41.2	17.8	62.2	27.4	76.4	39.9	94.0	69.5	149
17	5.9	40.5	17.4	61.5	26.2	74.8	38.3	92.0	67.1	146
24	5.8	40.3	17.3	61.3	25.8	74.2	37.3	90.7	65.8	143

*General Radiological Heliophos. 2 peak. 0.3 mm and 1.0 mm focus.
†Siemens Gigantos. 12 peak. 0.6 mm and 1.0 mm focus.
‡Philips Maximus DLX. 6 peak. 1.0 and 2.0 mm focus.
§kVp relative to constant potential determined from the mean value of the emergent X-ray beam energy after attenuation by 1.5 mm Cu (0.6 mm Cu for 40 kV).

removed in order to allow maximum and minimum effective tube angle. The wide angle beam was reduced by a secondary collimator in order to eliminate extraneous radiation and limit the extra-focal radiation to that found in most modern X-ray tubes. Although the tubes examined were of different ages, one heavily used, all gave identical readings, and thus demonstrated that any target pitting was not having an adverse effect. Measurements of a target of a new demonstration portable X-ray generator gave agreement with the figures in Fig. 2.

In order, therefore, to eliminate error using inferential methods to check kilovoltage, the target angle of the tube to be examined should always match that used for calibration. The precision of calculation of inherent filtration is not affected if the same target angle is employed for both filtered and unfiltered exposures when using the method described by Ardran and Crooks (1972).

REFERENCES

Ardran, G. M. and Crooks, H. E., 1967. Diagnostic X-ray beam quality, *AERE Memorandum 1909*.
1968. Checking diagnostic beam quality. *British Journal of Radiology*, *41*, 193–198.
1972. The measurement of inherent filtration in diagnostic X-ray tubes and the effect of target angle on X-ray quality. *British Journal of Radiology*, *45*, 599–602.
Zintheo, C. J., 1937. Variations in the intensity and quality of roentgen ray output as affected by the angle to the central ray, the roentgen ray tube and the roentgen ray apparatus. *American Journal of Roentgenology*, *37*, 98–104.

A new ophthalmic ultrasonic B-scanner

By J. S. Paton, B.Sc., C.Eng., M.I.Mech.E., M. B. D. Cooke, B.A., M.Inst.P.

West of Scotland Health Boards, Department of Clinical Physics and Bio-Engineering, 11 West Graham Street, Glasgow G4 9LF

and G. R. Sutherland, M.B., F.R.C.P., F.R.C.R.

Department of Radiology, Stobhill General Hospital, Glasgow G21 3UW

(Received March 1979 and in revised form July 1979)

In ophthalmology the A-scan technique (Mundt and Hughes, 1956; Oksala and Lehtinen, 1958; Baum, 1958; Ossoinig, 1968) has enjoyed considerable success although this has been restricted to a comparatively small number of expert operators because of the technical difficulties in interpretation. Although an ophthalmic B-scanning unit had first been designed by Baum and Greenwood in 1958 no commercially available unit was available until 1969 when Coleman, Konig and Katz (Coleman *et al.*, 1969) introduced their combined A and B scan ophthalmic ultrasound apparatus. Since then comparatively inexpensive portable contact B-scanners have been developed (*e.g.* Bronson, 1974) which have given an impetus to the use of B-scan ultrasound in clinical practice.

However, as yet none of the major manufacturers of ultrasonic equipment apart from EMI Medical Ltd (Nuclear Enterprises Ltd) have taken an interest in the use of their equipment for ophthalmic scanning, despite the very large potential for the use of general purpose equipment installed in the majority of large hospitals in examinations of the orbit (Sutherland and Forrester, 1974; 1975a; 1975b; Forrester *et al.*, 1977; Sutherland, 1978.

Although the NE Diasonograph transducer assembly is suitable for ophthalmic scanning, other types of equipment using a "pendulum type" of transducer mounting are much less suitable. It was therefore considered worthwhile designing an ophthalmic scanning module which would be used in conjunction with different ultrasonic machines on a simple "plug-in" basis.

The Scanner

The scanner is shown in Fig. 1 and consists of a transducer, scanning head, head positioning assembly and support stand. The whole instrument is mounted on a base-board on which is also mounted a ring-clamp and stand which holds the water coupling bath.

The transducer

A special transducer was manufactured* for use with the instrument. This is a 5 MHz short-pulse (two to three cycles) unit using a focusing bowl element with an epoxy facing. The beam width at focus (4 cm), 6 dB below peak intensity, was measured by hydrophone as 1.96 mm. The range over which the intensity was within 6 dB of the focal peak was 2.2 cm to 7.5 cm. The 8 mm diameter crystal is mounted in a water-proof nylon housing.

The scanning head

The probe is mounted in a link mechanism designed to produce an oscillation of the transducer about a line on its front face through a total angle of 120 deg (60 deg either side of zero position). Because of the design of the linkage, there are no pivots near

---

*Transducer Manufacturing Services, Lauriston, Cowbridge Hill, Malmesbury, Wiltshire SN16 9LU.

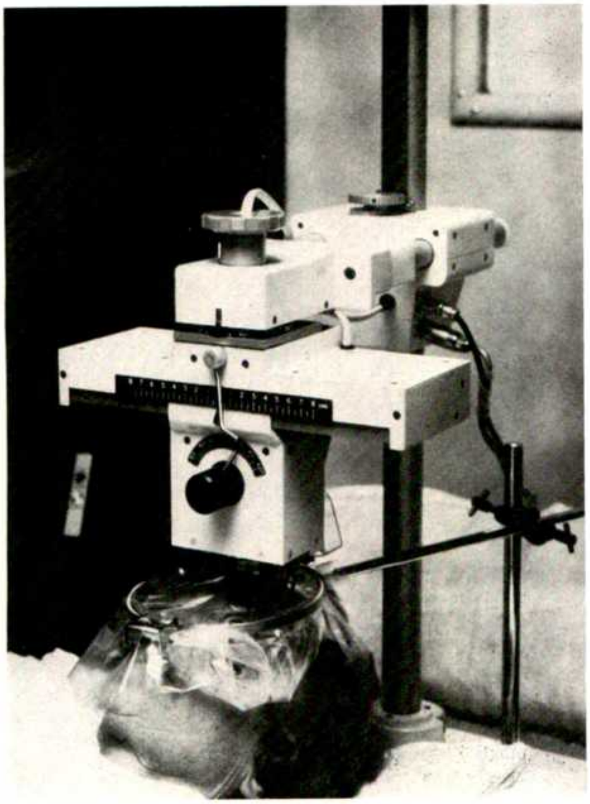


FIG. 1.

The scanner in position over the patient, ready to scan.

the transducer to limit access or visibility and so the probe can be accurately positioned very close to the patient if required, the part of the probe nearest the patient having minimum movement during oscillation. The control knob carries a pointer showing the angular position of the probe on a scale on the casing and a sine/cosine potentiometer supplies probe angle information to the display module. The linkage housing has a traverse travel of 160 mm (80 mm either side of mid-point). A multiturn potentiometer carried on the linkage housing and driven from a rack on the scanning head gives linear positional information to the display module. The underside of the linear track is protected by a bellows-type shutter mechanism which keeps dirt off the linear tracking and away from the precision rack and pinion. A hinged Perspex guard mounted on the linkage housing can be hinged down to protect the probe from mechanical damage when the instrument is not in use.

The scanning head can be moved easily by hand through a range of 38 mm in line with the control knob axis for fine selection of the scanning plane. This movement is controlled by a release lever above the control knob which can be progressively released to give variable frictional damping up to fairly firm locking. Finally, the entire head can be rotated about a vertical axis through a total of about 300 deg and locked at any position to allow any plane through the eye to be scanned from either side of the patient.

Scanning head positioning assembly

The scanning head can be moved to and from the stand through 114 mm by means of a handwheel on top of the main support carriage. The entire weight of carriage and head is counterbalanced and it can be wound up and down through 400 mm. The handle for this movement is located at the rear of the support carriage. This vertical movement is locked positively by means of a lever located next to the vertical winding handle. Finally, the entire column can be rotated freely through 360 deg about its base and locked at any position by means of a lever mounted on the column foot. The foot is bolted firmly to a base-board which slips between the top of the examination trolley and the foam pad on which the patient's head and shoulders are resting, thus anchoring the unit firmly.

Holder for the water coupling bath

The holder for the water coupling consists of an inner metal ring which can be positioned easily relative to the probe by means of a sliding clamp on a vertical pillar fixed to the base-board. An outer, spring-loaded expanding ring which has a rubber friction strip on its inner face acts as a clamp to the plastic water-bath bag. This bag is simply a sheet of polythene with an eye hole in the centre around which is a ring of doublesided self-adhesive material (3M "Stomaseal") which is stuck round the patient's eye. The patient then lies down in front of the scanner, the inner ring is positioned over the patient with the eye central, the polythene is draped over the inner ring and the outer ring is clipped in place.

ELECTRONIC INTERFACE

The ophthalmic scanner has initially been interfaced to an NE 4200 electronic module. Operating personnel make the change from the regular gantry to the ophthalmic unit by substitution of the transducer cable and a multiway connector mounted at the rear of the electronic module. No other adjustments are required.

A resistor network mounted inside the scanner connector provides a dummy Y position signal and a means to adjust the volts/mm output of the X movement to that obtained from the NE 4200 frame. The transducer rotation is sensed by a sine/cosine potentiometer and only requires mechanical alignment. Finally, to ensure correct image registration it is also necessary to correct for the fact that the scanner transducer rotates about an axis at its face, not several centimetres behind it. This is achieved by triggering the section-scan timebase with the "transmitter trigger" pulse instead of with the "section scan trigger" pulse. The switchover is controlled by a logic gate package enabled by a shorting link in the scanner connector.

The initial modification is easily carried out by an electronics technician and detailed advice is available from the authors. While the details given apply to the NE 4200, the same general principles may be applied to other manufacturers' equipment.

CLINICAL APPLICATIONS

The patient is prepared for scanning by cleaning the area around the eye. The scanning head and water bath are swung away from the table and the patient is positioned in front of the support column. The plastic sheet is stuck round the patient's eye, the ring positioned and the water bath prepared. Prewarmed Ringer's lactate is slowly poured down the side of the bath until it is filled to within a few millimetres of the ring edge. The scanning head is then swung into position and lowered until the transducer is completely submerged in the fluid and positioned centrally over the eye. The column rotation and vertical travel locks are then applied. Scanning can now proceed as with a normal B-scan system.

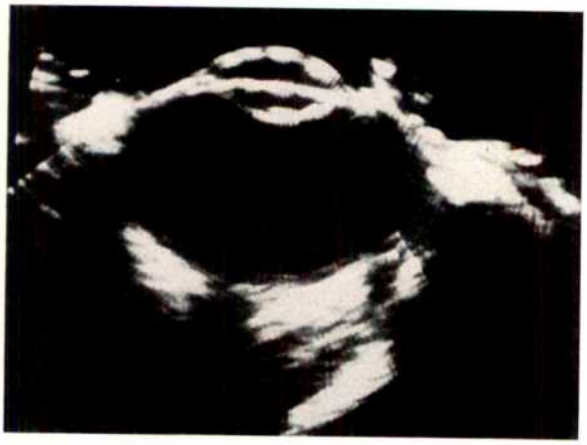


FIG. 2.

Typical eye scan using the new scanner.

At the present time the unit has been used in conjunction with an NE Diasonograph 4200. As the interfacing between the new scanning module and the original electronics has no effect on the performance of the equipment, it is a simple matter, taking a few seconds, to unplug the standard gantry and replace it with the ophthalmic scanner. The ophthalmic scanner, in addition to being more convenient because of its smaller size, produces scans of improved quality because of the method of pivoting the transducer which gives considerably better access to the orbits, particularly the anterior portions of the globe in the region of the ciliary body, and to the walls of the orbital cavity (Fig. 2). So far only a 5 MHz transducer has been used but future developments include the use of higher frequency transducers and the development of coupling interfaces to other ultrasonic machines.

ACKNOWLEDGMENTS

The authors wish to acknowledge the grant given for the development of this equipment by the Equipment Research Committee of the Scottish Home and Health Department. The construction work was carried out jointly by the Department of Clinical Physics and Bio-Engineering, West of Scotland Health Boards, and Messrs. Hermitage Engineering (Mansfield) Ltd, Mansfield.

REFERENCES

BAUM, G., 1958. The application of ultrasonic locating techniques to ophthalmology, *Archives of Ophthalmology*, *60*, 263–279.

BAUM, G. and GREENWOOD, I., 1958. The application of ultrasonic locating techniques in ophthalmology. *Archives of Ophthalmology*, *60*, 263—279.

BRONSON, N. R., II., 1974. Contact B-scan ultrasonography. *American Journal of Ophthalmology*, *77*, 181–191.

COLEMAN, D. J., KONIG, W. F. and KATZ, L., 1969. The hand-operated ultrasound scan system for ophthalmic evaluation. *American Journal of Ophthalmology*, *68*, 256–263.

FORRESTER, J. V., SUTHERLAND, G. R. and MACDONALD, M., 1977. Experimental vitreous haemorrhage echographic appearances. *Graefes Archiv Opthalmologie*, *204*, 101–112.

MUNDT, G. H. and HUGHES, W. F., 1956. Ultrasonics in ocular diagnosis. *American Journal of Ophthalmology*, *41*, 488–498.

OKSALA, A. and LEHTINEN, A., 1958. Absorption of ultrasound in the aqueous humour, lens and vitreous body. *Acta Ophthalmologica*, *36*, 761–768.

OSSOINIG, K., 1968. Ultrasonic diagnosis of ophthalmology. *Wiener Medizinische Wochenschrift*, *118*, 362–367.

SUTHERLAND, G. R., 1978. The contribution of echography in the diagnosis of proptosis. *British Journal of Radiology*, *51*, 116–121.

SUTHERLAND, G. R. and FORRESTER, J. V., 1974. B-scan ultrasonography in ophthalmology. *British Journal of Radiology*, *47*, 383–386.

1975a. Demonstration of abnormalities of the lens by echography. *British Journal of Radiology*, *48*, 1019.

1975b. Echography in the diagnosis and management of retinal detachment. *British Journal of Radiology*, *48*, 796.

1980, *British Journal of Radiology*, *53*, 31–33 JANUARY 1980

Technical notes

A broad band microwave applicator for heating tumours

By S. Szwarnowski, B.Sc., R. J. Sheppard, Ph.D. and E. H. Grant, Ph.D., A.K.C., F.Inst.P.
Physics Department, Queen Elizabeth College, London W8 7AH
and N. M. Bleehen, M.A., B.Sc., F.R.C.P., F.R.C.R.
Department of Clinical Oncology and Radiotherapeutics, Addenbrookes Hospital, Cambridge CB2 2QQ

(*Received February 1979 and in revised form May 1979*)

The applicator consists basically of a length of semi-rigid coaxial line cable (Americon) which is able to move along the inside of a hypodermic needle (Fig. 1). The cable is approximately 9.5 cm long and has an outer conductor with a diameter of 0.086 cm. The inner conductor has a diameter of 0.02 cm and projects 0.6 cm from one end of the cable (I, Fig. 1). The other end of the cable is soldered to a miniature plug A (Americon, ARMM series) which enables the applicator to be connected to a microwave generator operating at a frequency of 2.45 GHz. This connector (A) is supported on a brass collar B, connected to the piston C which is 2.3 cm long and 0.32 cm in diameter. The coaxial line cable is rigidly glued to the inside of C using an epoxy resin. The piston C moves inside a closely fitting cylinder F which has an external diameter of 0.71 cm and is 3.2 cm long. The screw E is used to clamp C and controls the distance to which the inner conductor projects from the end of the hypodermic needle H (gauge 0). An adjustable brass circular ring D acts as a stop and prevents the coaxial line from projecting too far out of the tip (I) of the needle (H). By loosening the grub screw G, the needle H can be removed when blunt and replaced by a new one.

Before insertion of the applicator into the tissue, the inner conductor is retracted into the body of the needle, for protection, as it is only 0.02 cm in diameter and is easily damaged if pressed against hard materials. The sharp point of the needle is used to penetrate the skin overlying the tumour, and once this is done the inner conductor of the applicator can safely be inserted into the relatively soft interior.

This probe does not radiate well in air, but in the tumour, where the wavelength is much smaller, about 90% of the available power is transmitted into it. The relative power radiated by the applicator can be adjusted by varying the length of the inner conductor projecting from the end of the needle (I in Fig. 1). The particular points of interest with this type of applicator are that the heating is fairly well

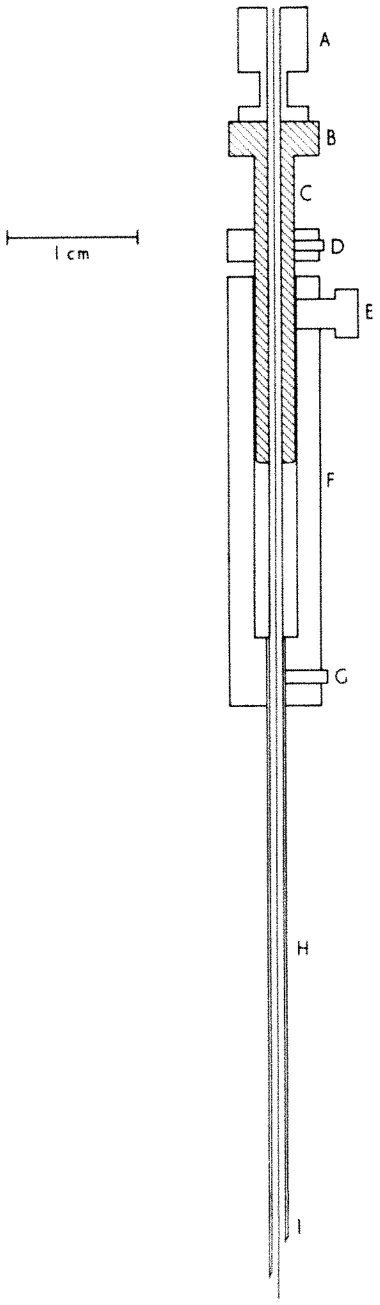


FIG. 1.
Coaxial line microwave applicator.

localized to the tumour, there are no losses due to absorption in the skin or intermediate material between the skin and the tumour, and only about two to three watts of power are required to produce the desired temperature (42–45°C). Also it is not necessary to restrict the operation of the applicator to a frequency of 2.45 GHz since it propagates the microwave via a coaxial line which is a broad band device, instead of with a waveguide which is narrow band.

An applicator based on a similar principle but without the advantages afforded by a retractable probe has been described by Taylor (1978a and b).

Performance of the applicator

To determine the type of heating pattern produced by the applicator, measurements were made of the temperature around the tip of the probe placed in phantom material·having electrical properties similar to muscle (Cheung and Koopman, 1976). A small

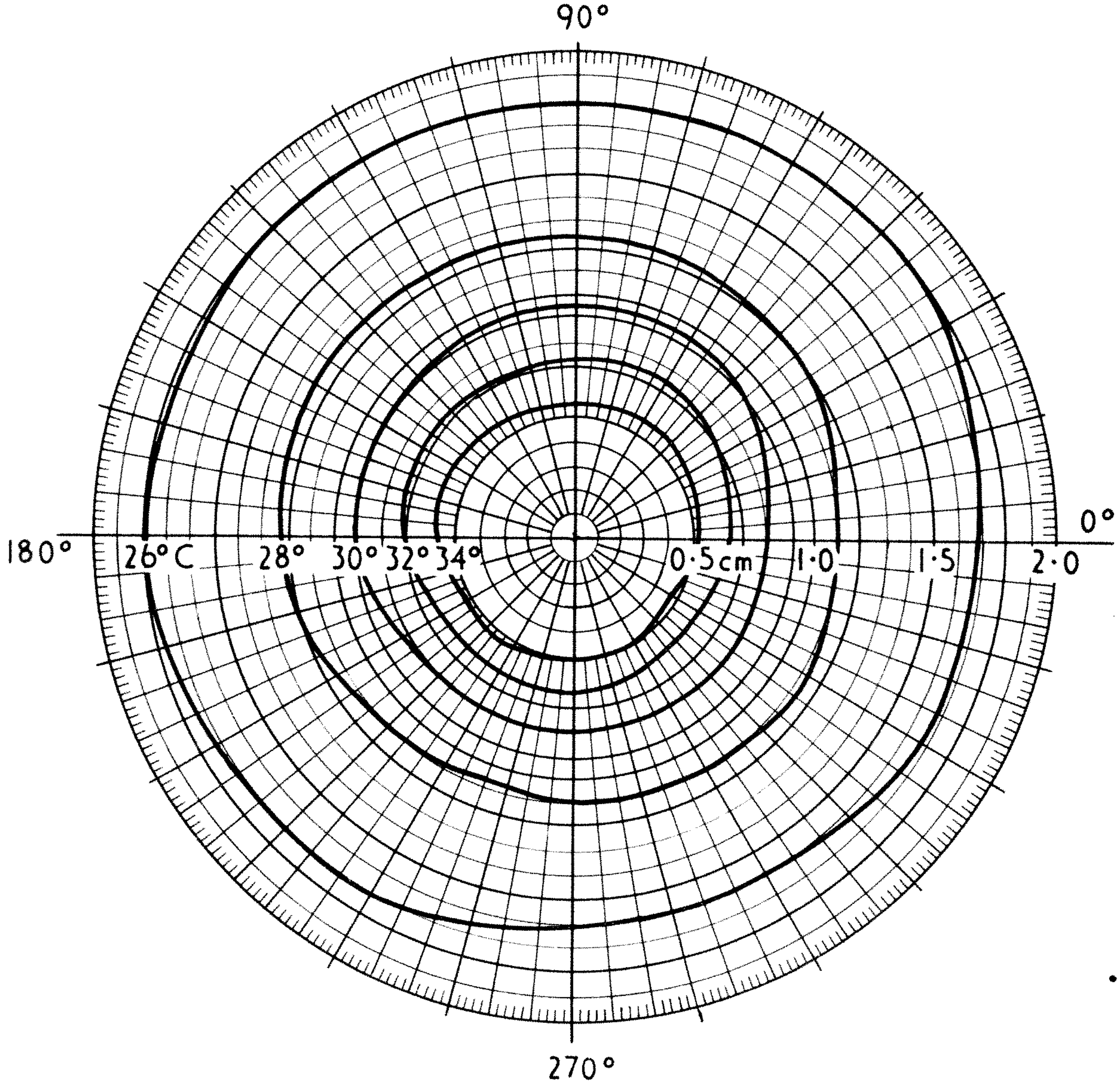


Fig. 2.

Heating pattern in phantom material.

thermocouple 8 cm long with a junction width of 0.012 cm, to be described elsewhere, was used to measure the temperature. No interaction between the microwave field and the thermocouple was observed (Szwarnowski *et al.*, in press).

The phantom material was placed in a hollow cylindrical container 7 cm high and 5.4 cm internal diameter. The lid of the container had a hole drilled through its centre to take the needle of the applicator. A series of smaller holes, concentric with and at various distances from the centre hole, were also made in the lid to take the thermocouple which was inserted into the phantom so that the thermocouple junction was level with the centre of the 0.6 cm length of inner conductor that projected into the phantom from the end (I, Fig. 1) of the needle H. Approximately five watts of power were fed to the applicator, and the phantom was heated to equilibrium from room temperature (~21°C) before temperature measurements were commenced. The results of the measurements are shown in Fig. 2, where the continuous lines represent isotherms separated by intervals of 2°C. The mouth of the needle is orientated along the 270 deg line. It can be seen from Fig. 2 that the isotherms are approximately concentric with the tip of the applicator, and that the temperature increases more rapidly with distance towards the centre of the phantom.

CONCLUSIONS

In this paper a coaxial-line miniature applicator is described which enables tumours to be irradiated with microwaves. The applicator has a retractable inner conductor which can protrude by a variable amount, thus enabling the power dissipation in the tumour to be optimized. Although the test results presented in this paper concern temperature distributions within a tissue-equivalent phantom, the applicator is currently being used to irradiate tumours on the flanks of mice.

For convenience the measurements have been carried out at 2.45 GHz but at present the electrical properties of tissue over a wide range of frequency are being measured in the authors' laboratory to determine the optimum frequency for such work. Since the applicator is a broadband device it would be operated at this frequency in experimental and clinical situations.

ACKNOWLEDGMENT

Thanks are due to the Cancer Research Campaign for supporting S.S. and for an apparatus grant.

REFERENCES

CHEUNG, A. Y. and KOOPMAN, D. W., 1976. Experimental development of simulated biomaterials for dosimetry studies of hazardous microwave radiation. *IEEE Transactions on Microwave Theory and Techniques, MTT-24*, 699–673.

GUY, A. W., 1971. Analyses of electromagnetic fields induced in biological tissues by thermographic studies on equivalent phantom models. *IEEE Transactions on Microwave Theory and Techniques, MTT-19*, 214–223.

HOLT, J. A. G., 1975. The use of VHF radiowaves in cancer therapy. *Australasian Radiology, 19*, 223–241.

JOHNSON, C. C. and GUY, A. W., 1972. Non-ionizing electromagnetic wave effects in biological materials and systems. *Proceedings of the IEEE, 60*, 692–718.

JOINES, W. T., WILSON, B. and SHARPE, S. M., 1977. *Temperature-controlled heating of tumours by microwaves.* Proceedings of Southeastcon '77 on Imaginative Engineering Thru Education and Experience, Williamsburg, Va, USA, 4–6 April 1977, 124–128.

LEHMANN, J. F., GUY, A. W., WARREN, C. G., DE LATEUR, B. J. and STONEBRIDGE, J. B., 1970. Evaluation of a microwave contact applicator. *Archives of Physical Medicine and Rehabilitation, 51*, 143–146.

LE VEEN, H. H., WAPNICK, S., PICCONE, V., FALK, G. and AHMED, N., 1976. Tumor eradication by radiofrequency therapy. *Journal of the American Medical Association, 235*, 2198–2200.

TAYLOR, L. S., 1978a. *Cancer Therapy by Hyperthermia and Radiation.* Proceedings of the 2nd International Symposium, Essen. June 2–4, 1977, 115–117.

1978b. Electromagnetic Syringe. *IEEE Transactions on Biomedical Engineering, BME-25*, 303.

WHALLEY, W. B., 1977. Radio frequency eradication of tumours. *Electronics and Power, 23*, 415–417.

SZWARNOWSKI, S., SHEPPARD, R. J., GRANT, E. H. and BLEEHEN, N. M., 1980. A thermocouple for measuring temperature in a biological material heated by microwaves. *British Journal of Radiology* (in press).

A technique for producing localized measurable hyperthermia in superficial rat tumours using ultra-high frequency currents

By P. B. Dunscombe, Ph.D. and B. M. Backhouse, M.B., B.S., F.R.C.R.

Departments of Medical Physics, Surgery and Radiotherapy, Charing Cross Hospital, London W6 8RF

(Received December 1978 and in revised form March 1979)

An increasing amount of evidence is becoming available from *in vitro* studies to indicate that elevated temperatures can enhance the damaging effect of ionizing radiation (*e.g.* Ben-Hur *et al.*, 1978). In this communication we describe a technique which allows the extension of such work to *in vivo* studies on rodents. Localized hyperthermia has been produced in tumours on the flanks of rats by the flow of an ultra-high-frequency current at 433.92 MHz. In addition, under our experimental conditions it has been possible to monitor the tumour temperature during heating.

As the work described here forms part of a project to assess the usefulness and feasibility of hyperthermic treatment of human cancers, the choice of frequency was based on its suitability for producing deep heat in man. Radiofrequency power can be introduced into the body in several ways. An electric field may be applied in a direction predominantly normal to tissue interfaces, as in short-wave diathermy. As a consequence of the boundary conditions and the electrical properties of tissues, such a technique results in a higher rate of heat production in tissues with low water content such as fat and bone than in those containing more water such as muscle. In contrast, microwave diathermy produces an electric field which is predominantly parallel to tissue interfaces. With this orientation of the electric field, fat and bone become relatively transparent to the radiation, with the advantage, therefore, that most of the energy is deposited in tissues with higher water content. A technique which has similar characteristics of power absorption is inductive short-wave diathermy, but the heating pattern is reported to be difficult to use for the treatment of small areas (Guy, 1976). The penetration of microwave radiation increases with decreasing frequency (Johnson and Guy, 1972) and so it is advantageous to use the lowest frequency for which suitable applicators can be obtained. At the moment the lowest frequency at which commercial microwave diathermy equipment operates is 433.92 MHz.

Whilst this frequency appears to be close to the optimum for microwave diathermy of humans, both the wavelength of the radiation and the applicators are far too large for the production of localized hyperthermia in rodents. For animal experiments, therefore, it is necessary to adopt the short-wave diathermy approach in which the part of the animal to be heated is placed between two current-carrying electrodes.

When a high-frequency alternating current is passed through tissue its energy is converted into heat through ohmic heating due to the resistance of the tissue and through the friction experienced by polar molecules such as water as they rotate in the changing field. Structures which project from the body, such as superficial implanted tumours, can be selectively heated by ensuring that the currents are restricted as far as possible to that structure. This is the principle upon which the technique to be described is based.

TECHNIQUES

Heating system

A 433.92 MHz generator (Erbotherm 69) was coupled to a rectangular waveguide, 52×35 cm, so as to excite it in a TE_{10} mode. This waveguide, which at one end was short-circuited and at the other filled with an absorbing material, not only reduced the amount of stray radiation but also ensured that the electromagnetic wave was plane polarized which, as described below, allowed temperatures to be monitored during heating. A significant degree of reflection was produced at the absorber resulting in the formation of a standing wave within the guide.

The high-frequency current was produced from the electromagnetic field by placing an aerial, which was capacitively coupled to the tumour, at a standing wave maximum inside the guide, 120 cm from the absorber. The dipole aerial consisted of two conducting rods 17 cm long ending in discs 7 mm in diameter. A 2 mm thick Perspex spacer separated the disc from the tumour to avoid skin burns. The anaesthetized animal was held in position on a specially designed table (shown in Fig. 1) by netting stretched loosely over it. Such a system should not impair the blood flow to the tumour.

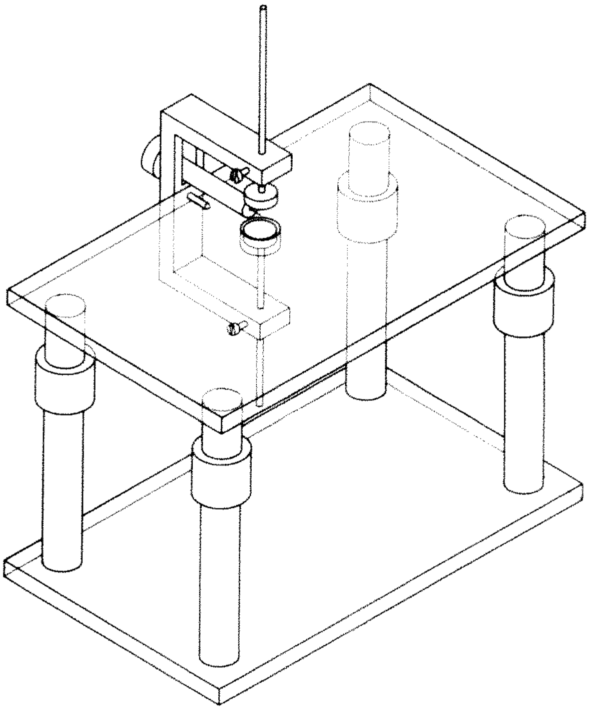


Fig. 1.

The heating system for rat tumours showing the aerials and the thermocouple probe. This was positioned at a standing wave maximum inside the waveguide.

As already pointed out, a characteristic of radiofrequency current heating produced by capacitive coupling to the tissue is that fat, due to its greater resistance, suffers a higher rate of rise of temperature than do tissues which contain more water. Although the magnitude of this effect decreases as the frequency increases, it is still large at 434 MHz. According to Schwan and Piersol (1954) a factor of three is involved at this frequency but more recent data (Johnson and Guy, 1972) indicate that, if cooling mechanisms are ignored, this factor could exceed ten. A further property is that the current density near the electrodes is higher than in the centre of the tumour, resulting in non-uniformity of the heating distribution. However, the high thermal conductivity of tissue results in a smoothing out of the internal temperature. A lower heating rate can be expected to assist the attainment of an even temperature distribution, but at the cost of reducing the degree of localization as heat is transported to neighbouring tissue by the blood.

Temperature measurement

Due to their small size and ease of handling, thermocouples were chosen as the temperature-measuring devices. Tumour temperature was monitored during heating by a thermocouple constructed from 51 μm diameter wires and housed in a 26 G (0.46 mm diameter) needle. The thermocouple voltages were fed directly to a sensitive chart recorder 8 m away in an adjacent room. The jig holding the probe and dipoles was designed so that the tip of the needle was on the axis of the dipoles. A rectal probe of similar design but without the steel needle was used for later experiments. By ensuring that the metallic components of these devices were maintained in a position perpendicular to the electric vector of the plane polarized electromagnetic wave, direct pick-up of the field and consequent heating of the probes could be minimized.

RESULTS

In vitro

A Smiths Pyroscan, modified for line scanning (Wheldon, 1977), was used to investigate the temperature distribution produced by the heating system. Tissue-equivalent gels, made according to the recipe of Guy (1971), were heated for two minutes and scanned 40 seconds later with the results shown in Figs. 2 and 3. For both these scans the gels were constructed in two halves with the plane of contact either normal (Fig. 2) or parallel (Fig. 3) to the axis of the aerial. These two halves were separated immediately before scanning. Due to the spatial resolution of the scanner, about 3 mm, the dimension of the gel used to determine the temperature profile along the axis of the dipoles was larger than that of the tumours treated. On this scan the increased heating near the dipoles is clear.

The scans shown in Figs. 2 and 3 are intended to indicate the distribution of heat production and were obtained by rapidly heating the gel; absorbed power

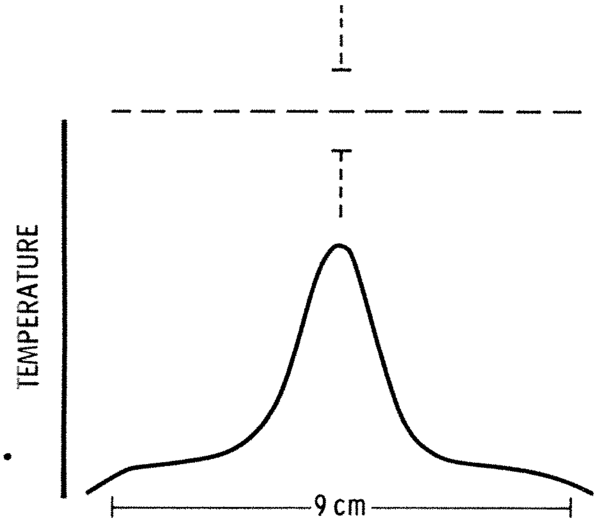


FIG. 2.

Temperature profile in a tissue-equivalent gel in the plane midway between the aerials and normal to their axis. Due to the absence of emissivity data for the gels it is not possible to calibrate the temperature scale.

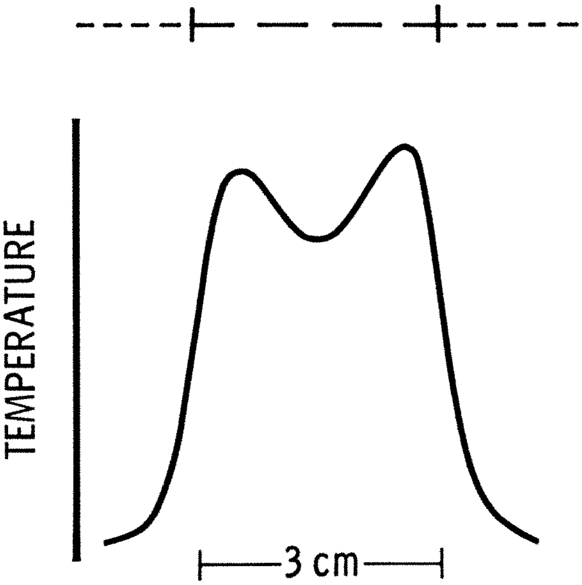


FIG. 3.

Temperature profile in a tissue-equivalent gel in a plane containing the axis of the aerial.

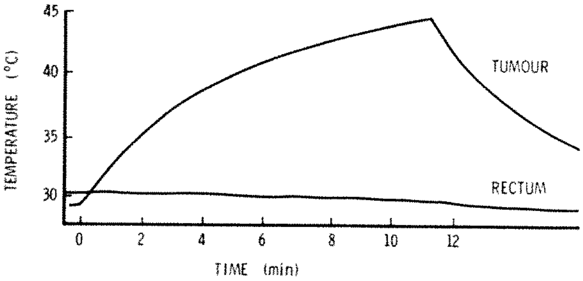


FIG. 4.

Rectal and tumour temperatures in a dead rat at approximately two-thirds of maximum power.

densities in the centre of the gels were in the region of 125 W/kg. When, however, the system was used to maintain a steady mid-gel temperature for 20 minutes by controlling the generator power, the surface peaks of Fig. 3 disappeared indicating the uniformity of temperature obtainable when the rate of heat production in the gel is low.

A thermographic technique, with an accuracy of 0.3°C, was used in an attempt to observe perturbation of the temperature pattern caused by the presence of the thermocouple probe. No effect was seen within the reproducibility of the scans which was about 20% for a mid-gel temperature rise of 5°C. Also, no difference in the final temperature of a gel was seen when it was heated with and without the probe in position.

In vivo

A small series of Wistar rats were subjected to the heating system described. The rats, carrying an RD3 tumour on the flank, were anaesthetized with 2.5 mg/kg Hypnorm administered intramuscularly, before being mounted in the apparatus. Heating and cooling rates were studied in both live and dead animals. Figure 4 shows the tumour and rectal temperature during heating at a mid-tumour absorbed power density of 240 W/kg in a dead rat. A small amount of pick-up of the electromagnetic field is just discernible on the rectal monitor.

At distances of 1 and 2 cm from the axis of the aerials the heating rates in dead rats dropped to 55% and 40% respectively of that in the tumour centre. These figures, which are higher than those expected from the measurements in the gel, may be due to the thermal insulation afforded by the animal's fur.

The mean rates of tumour heating in 13 live and dead rats were 3.28±2.21 and 3.17±2.09°C/min respectively at 37°C. The large spread of results is thought to be largely due to the variation in tumour size with the larger tumours being heated more slowly, although some contribution can be expected to be due to uncertainty in the exact position of the thermocouple probe. The effect of repositioning the probe in two tumours in dead rats resulted in changes of measured heating rates of 14% and 3%. Cooling rates at 37°C did not show such a large temperature variation. Cooling rates in the live and dead animals were 1.44±0.41 and 1.16±0.49°C/min respectively. Power absorption in the live tumours was calculated from the specific heat of tissue to be 270±190 W/kg.

The data obtained allowed the ratio of the electrical conductivities, which determine the power absorption, to be calculated in the live and dead animal assuming no change in specific heat. The equation connecting the rate of temperature rise, dT/dt, with the processes of heat production and loss is

$$c\frac{dT}{dt} = \sigma E^2 + W_\mathrm{m} - W_\mathrm{b} - W_\mathrm{c}$$

where c is the specific heat of the tissue; σ is the conductivity of the tissue; E is the field strength; and W_m, W_b, W_c are the contributions from metabolic heat production, blood flow and thermal conduction.

The ratio of the elctrical conductivities in the live and dead tissue is given by

$$\frac{\sigma_\mathrm{l}}{\sigma_\mathrm{d}} = \frac{c_\mathrm{l}\left(\dfrac{dT}{dt_{\mathrm{l,r}}} - \dfrac{dT}{dt_{\mathrm{l,f}}}\right)}{c_\mathrm{d}\left(\dfrac{dT}{dt_{\mathrm{d,r}}} - \dfrac{dT}{dt_{\mathrm{d,f}}}\right)}$$

where the subscripts denote live (l) and dead (d) animals. r and f denote the temperatures rising (with the σE^2 term) and falling (without the σE^2 term). The mean of these results, 1.14±0.07 (standard error of the mean), does not indicate a significant change in electrical conductivity on death of the animal if it can be assumed that the specific heat is constant.

In no case was an effect of vasodilatation on tumour temperature observed (Lehmann *et al.*, 1969), presumably owing to the vascular organization of the tumour.

ACKNOWLEDGMENT

The authors are grateful to Rank Stanley Cox Ltd. for supplying the generator and for some financial support.

REFERENCES

BEN-HUR, E., ELKIND, M. M. and RIKLIS, E., 1978. The combined effects of hyperthermia and radiation in cultured mammalian cells, in *Cancer Therapy by Hyperthermia*, ed. C. Streffer (Urban and Schwarzenberg, Baltimore), pp. 29–36.

GUY, A. W., 1971. Analyses of electromagnetic fields induced in biological tissue by thermographic studies on equivalent phantom models, *Institute of Electrical and Electronic Engineers Transactions on Microwave Theory and Techniques, MTT-19*, pp. 205–214.

1976. Physical aspects of the electromagnetic heating of tissue volume, in *Proc. of the International Symposium on Cancer Therapy by Hyperthermia and Radiation*, eds. M. J. Wizenberg and J. E. Robinson (American College of Radiologists, Bethesda), pp. 179–192.

JOHNSON, C. and GUY, A. W., 1972. Nonionizing electromagnetic wave effects in biological materials and systems, in *Proceedings of the Institute of Electrical and Electronic Engineers, 60*, pp. 692–718.

LEHMANN, J. F., DE LATEUR, B. J. and STONEBRIDGE, J. B., 1969. Selective muscle heating by shortwave diathermy with a helical coil, *Archives of Physical Medicine and Rehabilitation, 50*, 117–132.

SCHWAN, H. P. and PIERSOL, G. M., 1954. The absorption of electromagnetic energy in body tissues, *American Journal of Physical Medicine, 33*, 371–404.

WHELDON, A. E., 1977. The application of linear thermographic scanning to the detection of deep venous thrombosis, M.Sc. Thesis, University of London.

Book reviews

Atlas of Nuclear Medicine. Volume 4. Bone. By P. E. Dibas and H. N. Wagner, pp. 196+181, illus., 1978 (W. B. Saunders Co., London), £24·50.
ISBN 0-7216-3001-4

A well-cultivated museum should provide the student or visitor with a distillation of the accumulated experience of the department housing it. An atlas may be regarded as a condensation of a museum, with more stringent limitations of space and available to a much larger, unselected audience. It should, therefore, contain examples indicating the range and variety of normal appearances, sufficiently annotated to ensure that the reader is aware of salient features, and proven examples of abnormal conditions. In view of the limitations of space, rarities can be justified only if they provide exercises in observation and logical deduction.

This atlas succeeds on most counts. A wide variety of normal and common abnormal appearances are clearly illustrated, captions are clear and concise and there is a good index. Inevitably there are deficiencies. The limited space available to paediatrics gives a misleading, oversimplified impression of the difficulty of interpreting the bone scan in children—it would be better for paediatrics to have been omitted from this volume altogether and made the subject of a separate volume. The description of metabolic bone disease is out-of-date and incomplete, and the documentation of some examples of less common conditions leaves the reader unconvinced and dissatisfied.

Despite these criticisms, even the most experienced worker cannot fail to learn something from this volume. Every department should have a good atlas of bone imaging. This is not the only such atlas, but none should be purchased until it has been compared with this one.

M. V. MERRICK.

Computed Tomography of Abdominal Abnormalities. By J. Haaga and N. E. Reich, pp.xi+430, 1978 (The C. V. Mosby Company, St. Louis), £34·40.

This book is a comprehensive practical guide to whole-body CT scanning of the abdomen and pelvis. The first chapter consists of a brief description of the physical principles of CT, followed by a general discussion on CT interpretation, including the use of window adjustments, contrast medium and methods employed to reduce artefacts. The remainder of the text is largely devoted to a description of CT appearances in various abdominal and pelvic conditions and to the indications for scanning. The subject has been considered according to anatomical site and each chapter includes sections on CT anatomy and specific aspects of examination technique.

There are over 400 illustrations of CT images. Line diagrams have only been included where necessary to clarify certain points. These illustrations amply support the text and the only criticism which might be made relates to the quality of the CT images which have been obtained with a 20-second scanner. However, the authors refer to this drawback in the final chapter in which they illustrate images taken with fast scanners (2–4 second scan times). This emphasizes the rapidly changing technology of whole-body CT. These final comments provide a synopsis of the state of the art just before publication and indicate future directions of development.

This book can be highly recommended to all radiologists involved in the work of whole-body CT. It should be a valuable day-to-day handbook, not only to those with limited experience but also to those who have already gained considerable expertise in this field.

JANET E. HUSBAND.

1980, *British Journal of Radiology*, *53*, 38–39

Case reports

Combined endoscopic and percutaneous trans-cystic approach to a retained common duct stone

By R. R. Mason, F.R.C.S., M.R.C.P. (UK), D.M.R.D. and P. B. Cotton, M.D., F.R.C.P.

Department of Radiology and Gastrointestinal Unit, The Middlesex Hospital, Mortimer Street, London W1N 8AA

Two techniques for the removal of retained common bile duct stones after surgery, namely endoscopic sphincterotomy and percutaneous extraction, have been combined with a favourable outcome. The centenarian patient has been spared further surgery.

CASE REPORT

A 101-year-old demented female presented with empyema of the gall-bladder; cholecystostomy was performed, leaving a Foley catheter in the gall-bladder. Post-operative cholangiography via the catheter showed a calculus in the common bile duct (Fig. 1). Five weeks later, mucus was draining from the cholecystostomy and the common duct stone was still present. Further surgery was felt to be contra-indicated. Endoscopic sphincterotomy was unsuccessful because it proved impossible to pass the diathermy knife through the papilla into the lower bile duct. We then attempted to extract the stone percutaneously via the cystic duct, gall-bladder and cholecystostomy, a technique described by Mazzariello (1976). A guide wire was successfully introduced along the route described and the track dilated to red Kifa size (about 7 FG). Further progress was slow, partly owing to the patient's inability to co-operate. This technique also was abandoned, leaving the tip of the trans-cystic

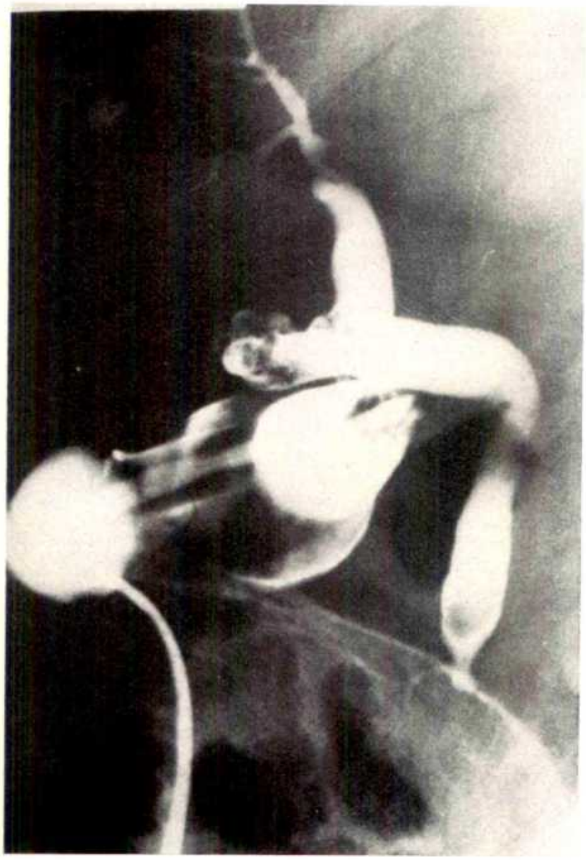


FIG. 1.

Post-operative cholangiogram via Foley catheter cholecystostomy showing calculus at lower end of common bile duct.

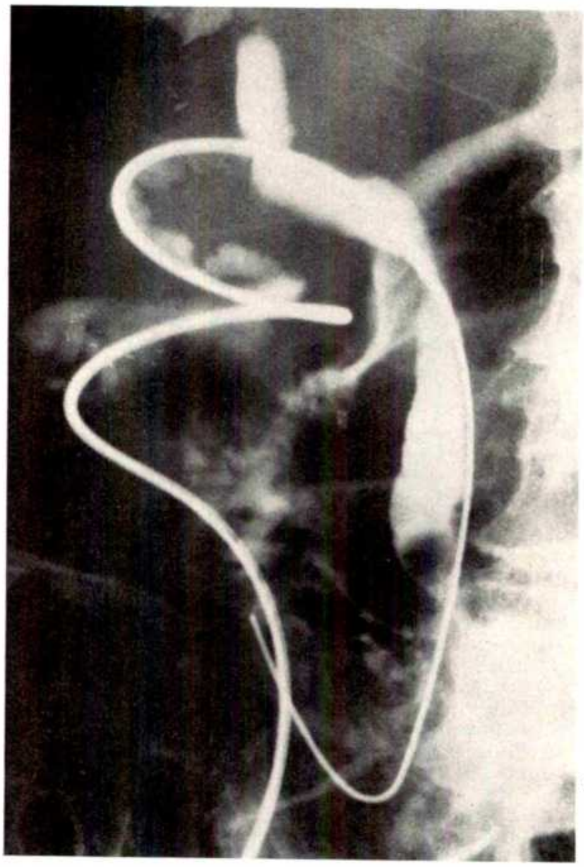


FIG. 2.

A guide wire has been passed along the cystic duct and common bile duct into the duodenum, and a catheter advanced over it into the bile duct.

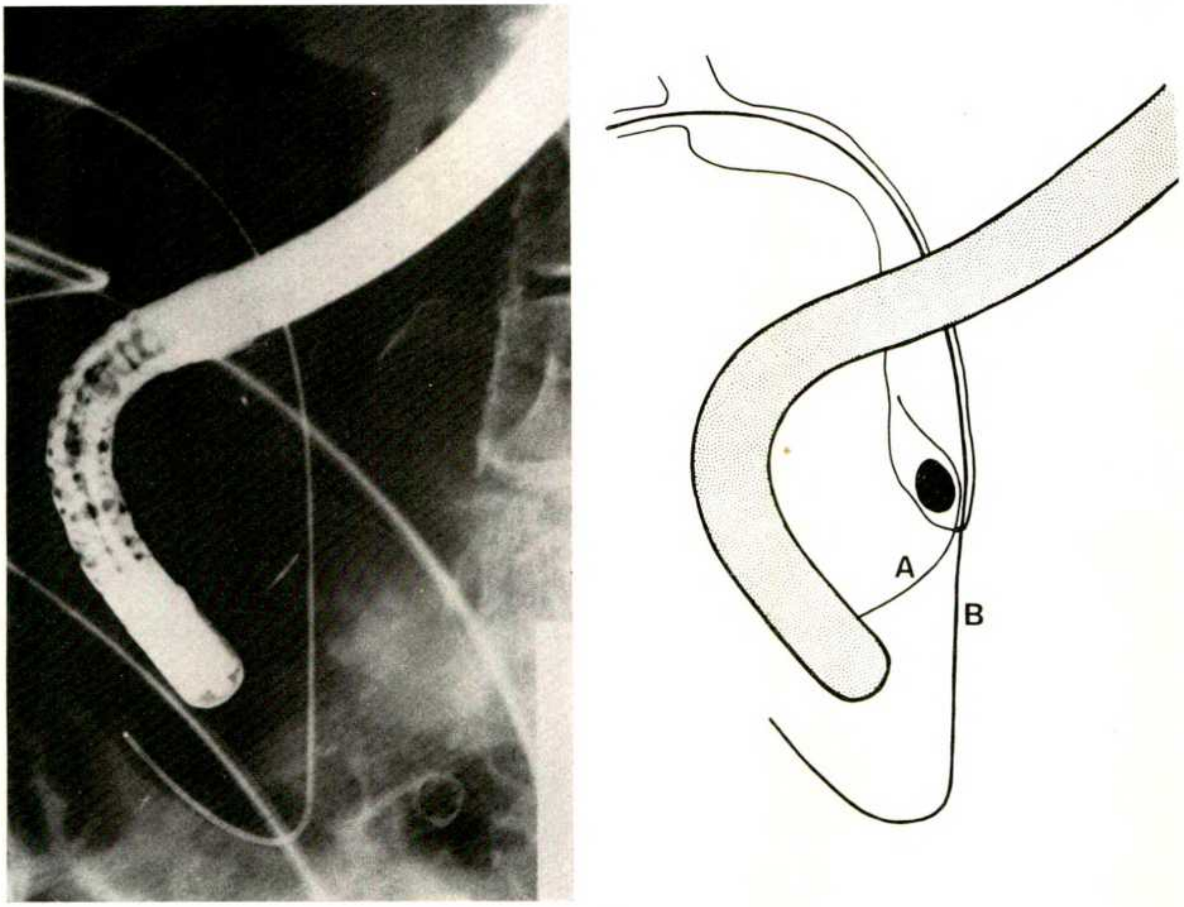


FIG. 3.

Radiograph taken at endoscopic sphincterotomy, and explanatory diagram. A—endoscopic diathermy wire. B—guide wire introduced percutaneously.

catheter in the common duct. A guide wire was then introduced through this catheter and advanced through the papilla into the duodenum (Fig. 2). At repeat duodenoscopy, the wire acted as a guide for the correct placement of the endoscopic diathermy knife into the lower bile duct (Fig. 3). The guide wire was withdrawn and sphincterotomy performed. The procedure was completed by flushing the stone through the sphincterotomy into the duodenum by injection of dilute contrast through the Kifa catheter under image-intensifier control.

DISCUSSION

For the management of retained common bile duct stones we favour percutaneous extraction (Mazzariello, 1976; Burhenne, 1974) when a suitable T-tube is present and endoscopic sphincterotomy when there is no tube (Cotton, 1979). In the unusual case described, neither technique alone was initially successful. Both techniques were combined to achieve a satisfactory result.

REFERENCES

BURHENNE, H. J., 1974. The technique of biliary stone extraction. *Radiology*, *113*, 567–572.

COTTON, P. B., 1979. Non-operative removal of bile duct stones by endoscopic sphincterotomy. *British Journal of Surgery* (in press).

MAZZARIELLO, R. M., 1976. Residual biliary duct stones: non-operative treatment of 570 patients. *Surgery Annual*, *Vol. 8*, 113–144. Appleton-Century-Crofts.

1980, *British Journal of Radiology*, *53*, 40–41

Case reports

De novo development of teeth in a teratoma

By Z. J. Ounjian, M.D., R. L. Mani, M.D. and J. R. Mani, M.D.

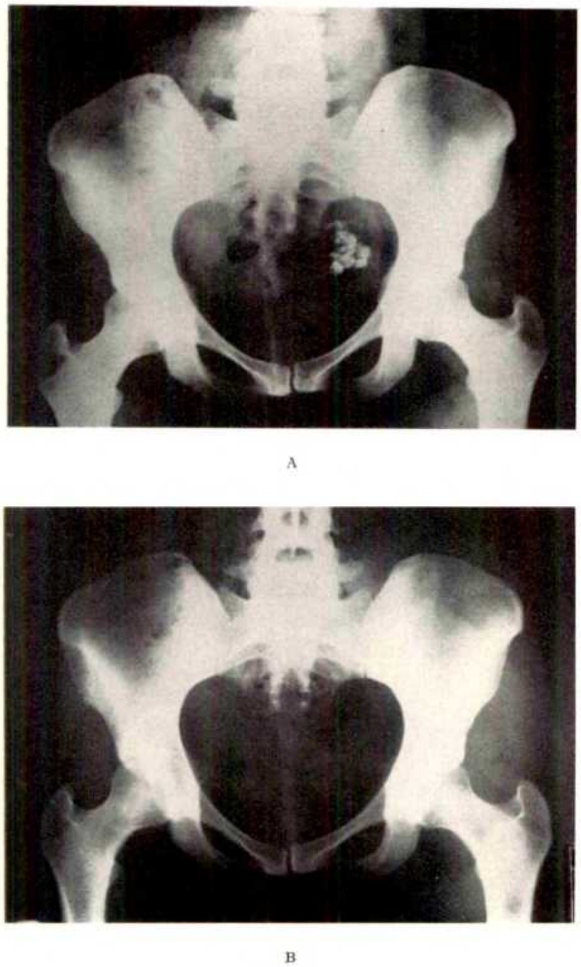
Departments of Radiology, University of California School of Medicine, Veterans Administration Hospital, and Franklin Hospital, San Francisco, California

(*Received May 1977 and in revised form May 1979*)

To our knowledge, *de novo* development of teeth in a teratoma has not been previously reported. The visualization of teeth in teratomas is a common occurrence, and sequential development of teeth adjacent to a previously existing one has been reported (Wollin and Ozonoff, 1961). This communication describes a patient who demonstrated radiographically the completely spontaneous development of multiple teeth in an ovarian teratoma.

Case Report

A 38-year-old woman was admitted to the hospital for evaluation of recurrent left hip and thigh pain. Family history was unremarkable. She had no symptoms of genito-urinary disease. A mass was palpable in the left lower quadrant of the abdomen and exhibited moderate tenderness and no rebound. A pelvic radiograph (Fig. 1A) revealed several teeth in the left pelvis that had not been seen on the same study done nine years earlier (Fig. 1B). At surgery, a 12 × 8 cm triloculated benign cystic teratoma was disclosed which contained mature elements of hair, skin, nervous tissue, retina, fat, and teeth. The right ovary was bivalved and noted to be normal. Subsequent to removal of the teratoma, the patient noted relief from previous left hip and thigh pain.

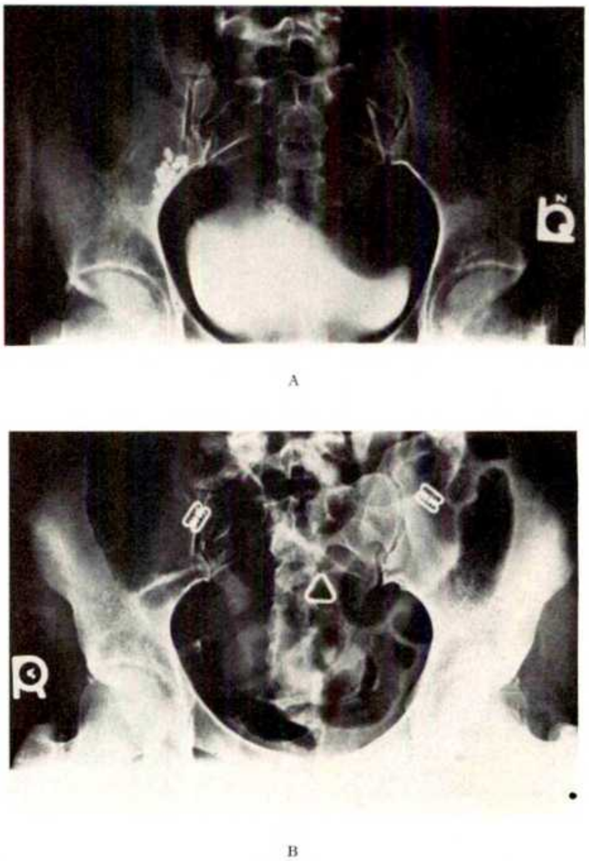


A

B

Fig. 1.

(A) Antero-posterior pelvic radiograph (1976) demonstrating several teeth in left pelvis. (B) Antero-posterior pelvic radiograph (1967) showing no teeth.



A

B

Fig. 2.

(A) Antero-posterior pelvic radiograph (1976) demonstrating multiple teeth in right pelvis. (B) Antero-posterior pelvic radiograph (1969) showing no evidence of teeth. This case was not proved surgically.

DISCUSSION

Growth of previously existing teeth in a teratoma has been described (Wollin and Ozonoff, 1961). What makes our case unique is the *de novo* development of teeth in a pelvic teratoma disclosed by two radiographs taken nine years apart. The mechanism of the hip and thigh pain on the appropriate side, relieved by surgical removal of the tumour, remains obscure. Possibly this large tumour (12 × 8 cm) pressed on adjacent sciatic nervous structures.

We have subsequently seen another case of apparently spontaneous development of multiple teeth in a right pelvic mass (Fig. 2A). A radiograph of the abdomen taken seven years earlier (Fig. 2B) showed no evidence of teeth in the pelvis. The tumour was not removed, however, so the diagnosis of pelvic teratoma can only be postulated from the radiographic evidence.

Teratomas of the ovary in women are often benign, whereas in men pelvic teratomas are frequently malignant (teratocarcinoma). Our case was of a typically large benign ovarian teratoma containing mature elements of all three embryonal layers and adds evidence to the concept that these tumours grow and mature.

REFERENCE

WOLLIN, E. and OZONOFF, M. B., 1961. Serial development of teeth in an ovarian teratoma. *New England Journal of Medicine*, *265*, 897–898.

Book reviews

Recent Advances in Radiology and Medical Imaging. 6. Edited by Sir Thomas Lodge and R. E. Steiner, pp. x+323, 1979 (Churchill Livingstone, Edinburgh), £18·00.
ISBN 0-443-01864-2

The change in title of this the sixth in this series indicates the increasing involvement of radiology in clinical diagnosis; this in turn imposes greater need for radiologists to keep abreast of current development and to be aware of possible lines of future progress.

The Editors, Sir Thomas Lodge and Professor R. E. Steiner present a well-selected and comprehensive series of articles by 20 authors—all recognized authorities in their fields. The articles are clearly written, well illustrated with up-to-date bibliographies. Despite the multi authorship there is an evenness of style and presentation which is commendable. As befits its current position in diagnostic radiology, the first three chapters are devoted to computerized tomography—Kreel and du Boulay covering the general and neurological aspects and Pullan its scientific basis. General radiology is covered by articles on the stomach, colon and liver, the pituitary, bone necrosis, rheumatoid arthritis, cardiology and paediatrics.

There is a particularly interesting article on urodynamics by Professor Thomas Sherwood which answers many of the questions raised in cases of urinary obstruction and bladder dysfunction.

The remaining five chapters deal with nuclear medicine and ultrasound—they provide detailed up-to-date indication of the usefulness of these methods in clinical radiological investigation.

This edition like its predecessor is excellent value at £18 and can be highly recommended to all who wish to read of current practices in the field of medical imaging.

J. A. GLEESON.

Fundamentals of Abdominal Sonography. A Teaching Approach. By Howard W. Raymond, 1979, pp. xii+723, (W. B. Saunders Co. Ltd., Eastbourne), £45·50.
ISBN 0-7216-5734-6.

This short 200 page text is divided into seven chapters covering the basic straightforward ultrasound examinations of the abdomen excluding the pelvis. There are almost 300 illustrations of presentable quality. The author is a general radiologist in a moderate-sized community hospital and presents a logical and practical balance to the use of ultrasound in abdominal problems. The format for each chapter consists of a basic lesson in technique, indications and findings followed by a series of case reports to test oneself using not only ultrasound scans but X-ray films and isotope scintigrams where appropriate. These represent the authors extensive involvement in patient management decisions. There is a bibliography at the end of each chapter.

There are many practical hints for the uninitiated with particular stress on the use of the semi-decubitus patient position for upper abdominal longitudinal scanning. The illustrations are of mixed format, some with white backgrounds and the rest with black. The author argues that this represents his practice and although it crosses the desires of those who wish to standardize us all it is a view with which I have much sympathy. Understanding of the basic principles behind each scan avoids any confusion.

There is little mention of the additional information obtainable by real time scanning of the abdomen. This and an additional chapter on general pelvic problems would add further strength to the book.

This is worthwhile reading for all ultrasonographers particularly those in early training, and would be a useful addition to undergraduate medical school libraries.

B. AYERS.

1980, *British Journal of Radiology*, *53*, 42

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Results of treatment of cancer of the cervix at Addenbrooke's Hopital, Cambridge, 1946–70

THE EDITOR—SIR,

We have recently analysed the survival results for 1234 cases of carcinoma of the cervix registered at the Radiotherapeutic Centre, Addenbrooke's Hospital, Cambridge in the period 1946–70. All patients referred to the Centre have been included except patients (a) classified as stage 0 (b) unstaged and (c) without histological confirmation. In five successive quinquennia from 1946 to 1970 the numbers of patients falling in categories (b) and (c) above were 27, 20, 14, 11 and 11. There were only nine patients classified as stage 0 from 1946 to 1960, but 64 and 186 respectively in 1961–65 and 1966–70 reflecting the introduction of cytological screening in the area during the early sixties. The patients have been re-staged uniformly on the basis of the definitions set out in the Handbook to the Stockholm Report (1974).

The age distribution of the patients changed very little over the period although the trend was for the average age to become lower. Fifty-five percent were under 55 years of age in 1966–70 compared with 50% in 1946–50, the increase being almost entirely in the 45–54 year age-group.

The overall stage distribution was 35.0, 46.1, 15.4 and 3.5% in stages I to IV respectively. The percentage of stage I patients increased from 27% in 1946–50 to 44% in 1966–70, most of this increase occurring after 1960. The increase was at the expense of the stage II cases since the percentage of patients in stages I and II combined remained around 80% throughout the period.

The primary treatment for stages I–III was usually intracavitary radium combined with external beam therapy. In stage IV cases, the treatment was almost always palliative. Primary surgery was performed in cases with unusual histology or vaginal stenosis, in some cases aged under 30 years and in a few for psychological reasons. Where possible, surgery was carried out in radio-incurable cases and sometimes after incomplete radiotherapy.

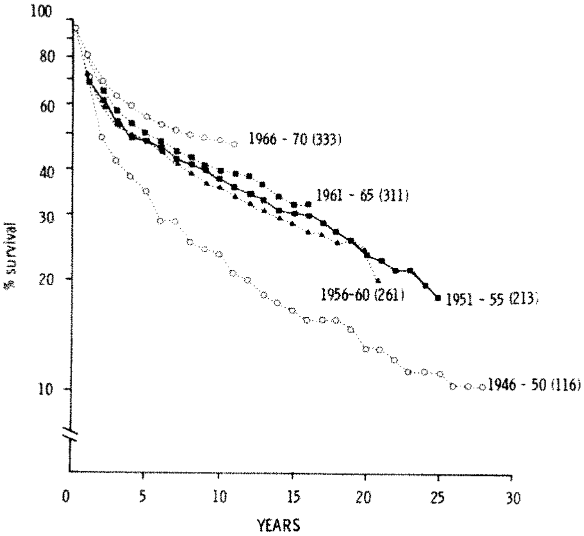


FIG. 1.

Results of treatment of Ca uterine cervix at Addenbrooke's Hospital, Cambridge, in quinquennia from 1946 to 1970.

Figure 1 shows the number of patients and the survival curve for each quinquennium from 1946–50 (116 patients) to 1966–70 (333 patients). The results improved markedly between 1946–50 and 1951–55, remained about the same level in 1956–60 but showed a further trend of improvement in 1961–65 and 1966–70. The five-year survival rates in successive quinquennia were 34.5, 47.0, 46.7, 49.5 and 55.6% respectively. A test for trend on these curves is highly significant ($\chi^2=23.7$; $P<0.005$), showing a real improvement in survival rate over the period. The trend is still significant when the 1946–50 group is excluded.

To see whether this could be accounted for solely by the change in stage distribution referred to above, the stage I and stage II cases were analysed separately. The trend was still significant in stage I cases ($\chi^2=15.1$, $P<0.05$ for all five quinquennia; $\chi^2=4.34$, $0.05>P>0.025$ when the 1946–50 group was excluded), but in the stage II cases it was only significant if the 1946–50 group was included ($\chi^2=5.87$, $0.025>P>0.01$) and there appears to have been no improvement over the last four quinquennia. Results in stage III have shown little change throughout the period with a five year survival rate of about 20%.

We conclude therefore that the overall improvement in results is not due to a change in the stage distribution, and has mainly occurred in stage I cases. Mould and Staffurth (1979) have recently reported a similar trend when comparing results from the Royal Marsden Hospital for the period 1962–70 with those for an earlier period, 1944–60.

Yours, etc.

MARY MITCHELL,
J. S. MITCHELL,
J. L. HAYBITTLE.

Radiotherapeutic Centre,
Addenbrooke's Hospital,
Hills Road,
Cambridge CB2 2QQ.

(*Received August 1979*)

REFERENCES

Handbook for the guidance of collaborators when reporting cases of carcinoma of the cervix, carcinoma of the corpus and carcinoma of the vagina (2nd revised edition), 1974. Editorial office: Radiumhemmet, S-104 01 Stockholm 60, Sweden.

MOULD, R. F. and STAFFURTH, J. F., 1979. Carcinoma of the cervix at the Royal Marsden Hospital, London, 1962–70: survival results. *British Journal of Radiology*, *52*, 157–158.

Dosage in high-energy electron therapy

THE EDITOR—SIR,

In their recent paper on the treatment of difficult cutaneous carcinomata with electrons (Grosch and Lambert, 1979), the authors state that "the given doses are similar to those used with photons".

This casual comment ignores one very important aspect of high-energy electron therapy. Megavoltage electrons have an RBE which is not significantly different from megavoltage photons (Williams and Hendry, 1978) but which is certainly different, and significantly lower, than the RBE of the low kilovoltage X-ray therapy normally used to treat skin carcinomata (Greene *et al.*, 1962).

More than 200 patients have received radical radiotherapy with 10 MeV electrons at the Christie Hospital over the last decade, many for ear lesions similar to the one described by Grosch and Lambert. Skin reactions were noted to be more severe or more prolonged if the tumour dose was adjusted to allow for the lower RBE of the electron beam. This altered tolerance is believed to be a consequence of the very different distribution of energy in the tissues by the two types of beam therapy.

In clinical practice now a reduction in dosage of 10% is made and this produces normal reactions with good control rates. This fortuitously brings the doses down to the level of radical kilovoltage therapy.

The results of high-energy electron therapy are very satisfactory at specially selected sites—but only if the tolerance of the tissues is not exceeded.

Yours, etc.,
R. D. HUNTER.

Department of Radiotherapy,
Christie Hospital & Holt Radium Institute,
Withington,
Manchester M20 9BX.

(*Received July 1979*)

REFERENCES

GREENE, D., MASSEY, J. B. and MEREDITH, W. J., 1962. Revision of published RBE values. *British Journal of Radiology*, *35*, 721.

GROSCH, E. and LAMBERT, H. E., 1979. The treatment of Difficult cutaneous basal and squamous cell carcinomata with electrons. *British Journal of Radiology*, *52*, 472–477.

WILLIAMS, P. C. and HENDRY, J. H., 1978. The RBE of megavoltage photon and electron beams. *British Journal of Radiology*, *51*, 220.

Dose rates to staff in the event of failure of beam-control mechanism in cobalt-60 units

THE EDITOR—Sir,

The Code of Practice (1972) and the Recommendations of the Radiotherapy Apparatus Safety Measures Panel require cobalt-60 units to be constructed in such a manner that it is possible to shut the useful beam off manually in the event of failure of the normal beam-control mechanism. However, in many cases this device will be inaccessible to the radiographers because of the position of the head, and no general guidance has been given as to the correct procedure to be followed in these cases.

If mains supply is still available to the head and the other control circuits are functioning normally, it may be possible to rotate the gantry to a more convenient position from the radiographer's control desk. However, if the shutter failure is associated with total or partial mains failure this course of action will not be possible and the staff will be faced with the problem of evacuating the patient from the treatment room with the source exposed.

Some radiographers appear to have been taught that they must not enter a treatment room in any circumstances unless the shutter is in the safe position, and most staff appear to have little idea of the actual dose rates inside a treatment room due to scatter and leakage radiation. It seems desirable to establish an agreed standard procedure for each type of machine so that radiographers trained in one centre will not be confused by conflicting instructions when they are employed in another. In an attempt to ascertain the safest procedure for both patient and staff, some measurements have been carried out on a Mobaltron-80 unit in positions which would be occupied by radiographers attending to a patient on the treatment couch.

A phantom was used consisting of a polystyrene block 34 × 30 × 30 cm thick and the field size was set to 20 × 20 cm at 80 cm SSD. The measurements were carried out using LiF extruded ribbon dosimeters supplied and measured by the NRPB Scottish centre. These dosimeters were placed at heights ranging from 75 cm to 175 cm above the floor in four different positions, and measurements were made with the phantom irradiated, the phantom and treatment table moved out of the beam, and also with the collimators closed down to 4 × 4 cm. With the gantry set to 0 deg and 180 deg positions A and B were chosen, 100 and 50 cm respectively from the isocentre on a line perpendicular to the beam axis and the rotation axis of the machine. A gantry angle of 0 deg indicates that the beam is pointing vertically downwards. In some treatment rooms access to the emergency shutter control may also be restricted when the gantry is set at 90 deg or 270 deg owing to the head passing too close to the wall. In order to provide similar data in this situation, positions C and D were chosen 100 cm and 50 cm respectively from the isocentre on a line between the treatment head and the couch at 45 deg to the beam axis and the rotation axis of the machine.

The results are given in Tables I and II. Dose rates are in mrad min^{-1} and have been normalized to an output of 100 rad min^{-1} at 80 cm SSD for a 10 × 10 cm field. The size of

TABLE I

DOSE RATE IN mRAD MIN^{-1}

	Gantry angle 0 deg			Gantry angle 180 deg		
Height (cm)	Phantom irradiated	Phantom removed	Collimators closed	Phantom irradiated	Phantom removed	Collimators closed
Position A						
75	186	101	17	67	26	16
95	130	88	22	81	40	19
115	114	72	22	104	49	21
135	92	49	21	139	66	18
155	70	32	24	195	90	17
175	51	19	15	217	116	14
Position B						
75	800	566	55	280	85	76
95	830	552	54	463	268	71
115	671	467	48	640	372	43
135	416	292	77	812	488	45
155	221	105	80	705	490	47
175	119	47	48	548	471	43

1980, *British Journal of Radiology*, *53*, 44–45

TABLE II

DOSE RATE IN mRAD MIN^{-1}

Gantry angle 90 deg			
Height (cm) Position C	Phantom irradiated	Phantom removed	Collimator closed
75	60	21	20
95	76	24	26
115	78	30	36
135	67	27	30
155	62	24	20
175	54	21	16
Position D			
75	214	108	67
95	386	141	106
115	495	257	77
135	496	262	84
155	288	118	87
175	150	73	54

TABLE III

DOSE RATE IN mRAD MIN^{-1} AT A HEIGHT OF 115 CM

Position and beam angle, deg	Measured	Calculated	Difference
	With phantom		
A 0	114	60	54
A 180	104	60	44
B 0	671	240	431
B 180	640	240	400
C 90	78	60	18
D 90	495	240	255
	No phantom		
A 0	72	20	52
A 180	49	12	37
B 0	467	32	435
B 180	372	12	360
C 90	30	9	21
D 90	257	12	245

the irradiation field was 20 × 20 cm except when the collimators were closed to 4 × 4 cm, the smallest field size for this type of machine.

Dose rates of radiation scattered from the phantom at a height of 115 cm have been calculated for position A, B, C and D using the data in ICRP Publication 3 (1960) Fig. 5 with the beam along the minor axis, and the corresponding dose rates without the phantom have been calculated from the data in British Standard 4094 Part 2 (1971), Fig. 19. The differences between these values and the measured dose rates at these points are shown in Table III. The IRCP values will not be strictly comparable because the masonite phantom consisted of an elliptic cylinder 36 × 20 cm whereas the present work used a polystyrene phantom of 30 × 30 cm cross-section, but the difference is not likely to be large.

It will be noted that the differences between the measured and calculated values for the two situations are in reasonable agreement. This suggests that the dose rates shown in the difference columns of Table III may be due to scatter from the collimator system. To test this, the measurements at a height of 115 cm in position D were repeated with the dosimeters exposed to collimator scatter but shielded by a 5 cm thick lead block from the radiation scattered by the phantom and the concrete wall. The normalized dose-rate was 220 mrad min^{-1} in both cases, which is in reasonable agreement with the difference figures of 255 and 245 mrad min^{-1} given in Table III, confirming that the collimator scatter can be an important source of stray radiation in the vicinity of the treatment head.

These results suggest that a reasonable emergency procedure might be first to move the patient out of the treatment beam by rotating the couch about the support column and then to close the collimators, thus reducing the dose rate to a low-level and allowing time for arrangements to be made to evacuate the patient. Of course, if the patient can walk, the second stage could be omitted. Tests have shown that it takes only five seconds for a radiographer to walk from the maze to the treatment couch and rotate it about its pedestal, and a further ten seconds for her to close the collimators from 20 × 20 cm to 4 × 4 cm.

The maximum permissible dose to the abdomen of women of reproductive capacity is given in Table B1 of the Code of Practice (1972) as 1.3 rem in any three months. In our experience radiographers working on Mobaltron-80 units normally receive doses of less than 20 mrem in any four week period. These measurements suggest, therefore, that there should be no difficulty in carrying out an emergency evacuation of a patient in a case of shutter failure without exceeding the maximum permissible dose.

I should like to thank Mr. A. Amos, chief technician in the department, for his assistance in carrying out the measurements.

Yours etc.,
C. BINKS.

Medical Physics Department,
St. Luke's Hospital,
Guildford,
Surrey GU1 3NT.

(*Received July 1979, revised September 1979*)

REFERENCES

Code of Practice for the Protection of Persons against Ionizing Radiations arising from Medical and Dental Use. HMSO 1972.

ICRP, 1960. *Protection Against X-rays up to Energies of 3 MeV and Beta and Gamma-rays from Sealed Sources*, Publication No. 3 (Pergamon Press).

British Standard 4094: Part 2 (1971).

Misonidazole also radiosensitizes some normal tissue

THE EDITOR—SIR,

Misonidazole is a radiosensitizer specific for hypoxic cells supposedly present only in tumours. We have been working with misonidazole in association with radiation, taking particular care to look for both local and general toxicity due to the drug *per se* and undesirable radiosensitization effects by the combined modality. We report here an increased mucosal reaction.

Ten patients with multiple neck node metastases from head and neck tumours were treated with multiple daily fractionation (MDF) radiotherapy (2+1.5+1.5 Gy/day, 4 h interval between fractions, 5 days/week) in association with misonidazole (1.2 g/m^2 per day, administered 2 h before the first daily fraction, up to a maximum dose of 12 g/m^2) (by courtesy of Prodotti Roche S.p.A., Milano, Italy). MDF is a new "concentrated" radiotherapy schedule, presently on trail in some European centres (Amsterdam, Leuven, Portsmouth, Rome). It is generally well accepted by the patients, with the exception of minor problems discussed elsewhere (Arcangeli *et. al.*, 1979). Patients were generally irradiated through an anterior field covering the whole neck with protection of the laryngeal region only. However, three patients were irradiated through two cross-firing fields to encompass both the primary and the neck nodes within the treatment area.

Contrary to expectation, almost no neurological symptons have been observed after misonidazole treatment. Only some mild nausea, easily controlled by metoclopramide, was present at the beginning in 8/10 patients, and some digital paresthesia was reported by one of the ten patients. No side effects were observed on the skin. No treatment has ever been discontinued because of these reactions. Misonidazole plasma levels were monitored in all patients and reached about 45 μg/ml 2 h after administration of the 1.2 g/m^2.

However, in the three patients undergoing irradiation (5.7 MV photons) with cross-firing beams, oropharyngeal mucositis has been observed earlier, longer, and to a higher degree than in patients treated with MDF alone. In these three cases, the treatment had to be discontinued after 25–30 Gy for as long as 2–3 weeks. It must be pointed out that none of these patients was a heavy drinker.

The present observations confirm the possibility of enhanced radiation damage to certain normal tissues when misonidazole is used (Hendry and Sutton, 1978; Horsney and Field, 1979), and suggest one of the following, non-mutually exclusive hypotheses: (i) misonidazole cytotoxicity is not, after all, highly selective against hypoxic tumour cells; (ii) some hypoxic cells are present in human oropharyngeal mucosa; (iii) misonidazole is interfering with radiation damage repair by normal cells during the relatively short fractionation intervals.

Our feeling is that misonidazole will be a useful addition to radiotherapy, provided a better understanding of its interaction at cellular and tissue levels is reached. Particular care with regard to side effects is necessary, especially when non-conventional fractionation is used in clinical radiotherapy.

Yours, etc.,
G. ARCANGELI,
C. NERVI,

Istituto Medico Scientifico,
Via L. Bodio, 58,
00191 Rome, Italy.

F. MAURO.

Lab. di Dosimetria e Biofisica,
Comitato Nazionale per l'Energia Nucleare,
00100 Rome A.D., Italy.

(*Received April 1979*)

REFERENCES

ARCANGELI, G., MAURO, F., MORELLI, D. and NERVI, C. Multiple daily fractionation in radiotherapy: biological rationale and preliminary clinical experiences. *European Journal of Cancer* (in press).

HENDRY, J. H. and SUTTON, M. L., 1978. Care with radiosensitizers. *British Journal of Radiology 51*, 927–928.

HORSNEY, S. and FIELD, S. B. 1979. The effects of single and fractionated doses of X-rays and neutrons on the oesophagus. *European Journal of Cancer*, *15*, 491–498.

Traumatic para-mediastinal air cysts

THE EDITOR—SIR,

In their recent article describing the radiographic features of post-traumatic para-mediastinal air cysts (Elyaderani and Gabriele, 1979) the authors state that "para-mediastinal air cysts have been noted only on the left side of the chest". In 1976 we (Ravin *et. al.*, 1976) reported three cases of post-traumatic air cysts, one of which (case 2) involved the right inferior pulmonary ligament. In addition, a second case thought to probably represent a right sided para-mediastinal pneumatocele has been reported by Fagan and Swischuk (Fagan and Swischuk, 1976). Thus, although para-mediastinal pneumatoceles seem to be more on the left side, they can occur, and have been reported, in the right pulmonary ligament as well. That this should occur is not surprising in as much as the ligaments are present bilaterally, although they may not be symmetrically developed in a given individual. Presumably a fully developed ligament is a prerequisite to development of a radiographically detectable para-mediastinal pneumatocele. The characteristic radiographic appearance of this benign lesion should allow the diagnosis to be made with reasonable certainty, although as indicated in many of the previous reports, it is necessary to perform an oesophagram to ensure that the oesophagus has not been ruptured.

Yours, etc.,
E. RAVIN.

Department of Radiology,
Duke University Medical Center,
Durham, North Carolina 27710 USA

(*Received September 1979*)

REFERENCES

ELYADERANI, M. K. and GABRIELE, L. F., 1979. Traumatic para-mediastinal air cysts. *British Journal of Radiology*, *52*, 458–460.

FAGAN, C. J. and SWISCHUK, L. E., 1976. Traumatic lung and paramediastinal pneumatoceles. *Radiology 120*, 11–18.

RAVIN, C. E., SMITH, G. W., LESTER, P. D., MCLOUD, T. C. and PUTMAN, C. E., 1976. Post-traumatic pneumatocele in the inferior pulmonary ligament. *Radiology 121*, 39–41.

1980, *British Journal of Radiology*, *53*, 46–49

Proceedings of The British Institute of Radiology

Preview of papers for the International Congress, Japan

Abstracts of papers presented at a Radiobiology Work-in-Progress Meeting of The British Institute of Radiology held on April 20, 1979 in the Reid-Knox Hall, Institute House, 32 Welbeck Street, London W1M 7PG.

Fast response methods in the radiation chemistry of lethal damage in cells, by B. D. Michael, H. A. Harrop and R. L. Maughan.
Effects of ionization equilibria on the radiosensitizing properties of nitro-imidazoles, by E. D. Clarke, R. S. Jacobs, C. E. Smithen, R. G. Wallace, P. Wardman, M. E. Watts and M. Woodcock.
Synthesis and evaluation of hypoxic cell sensitizers for clinical use, by I. J. Stratford.
Survival and transmission of symmetrical chromosomal aberrations, by J. R. K. Savage.
Some effects of hyperthermia on normal tissues, by S. B. Field, S. P. Hume and M. P. Law.
Dose rate effects in an irradiated post mitotic system, by R. W. Davies, A. J. Mill and J. V. Webb.
Response of an *in vivo–in vitro* tumour to X-rays and cytotoxic drugs: effect of tumour disaggregation method on cell survival, by J. S. Rasey and N. J. Nelson.
Recovery from sublethal damage by hypoxic tumour cells *in vivo* and *in vitro*, by N. J. McNally, K. C. George and J. de Ronde.
Response to single and fractionated radiation of jejunal crypts in mice treated with cytotoxic drugs, by J. V. Moore.
Effects of neutrons on normal tissues and tumours, by S. Hornsey.

FAST RESPONSE METHODS IN THE RADIATION CHEMISTRY OF LETHAL DAMAGE IN CELLS

By B. D. Michael, Hilary A. Harrop and R. L. Maughan

CRC Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

Radiobiology has stimulated research in certain areas of radiation chemistry, particularly the simulation in model chemical systems of the mechanisms of radiosensitization and radioprotection. However, attempts to investigate the radiation chemistry of the actual processes within intact cells, by direct observation of short-lived intermediates or by product analysis, are in general obscured by the very high ratio of non-lethal to lethal products of radiation. This problem has encouraged the development of fast-response methods which employ short pulses of radiation and can be used with intact cells and in which biological function is scored as an endpoint. Several such techniques exist and they rely upon the use of two time-separated probes (a radiation pulse and a fast change of concentration of a modifying agent such as oxygen) to follow the course of radiation-induced lethal events as a function of time. In general, the results that have been obtained with these methods tend to show a mixture of kinetic effects attributable both to the chemical reactions of interest and to diffusion of the modifying agent. However, one technique, the gas explosion method (Michael *et al.*, 1973), when used with bacteria, provides diffusion times that are sufficiently short compared with the times of some radiation-induced reactions of interest, that their reaction kinetics can be determined quite accurately. In *Serratia marcescens* we have been able to determine rates of the bimolecular reactions of various radioprotecting and radiosensitizing agents with target lesions. The reaction rates were found to be: dithiothreitol, 3.4×10^6; triacetoneamine-N-oxyl (TAN), 4.9×10^6; misonidazole, 4.6×10^4; oxygen, 2.8×10^8, all in $dm^3 \, mol^{-1}s^{-1}$. The rate of reaction with oxygen is much higher than the upper limit of 5×10^5 $dm^3 \, mol^{-1}s^{-1}$ for the reaction of oxygen with DNA radicals that has been determined by pulse radiolysis (Ward, 1978); this supports the view of Alper that O_2 does not sensitize by reacting directly with damaged DNA (Alper, 1977).

REFERENCES

Alper, T., 1977. The role of membrane damage in radiation-induced cell death. In, *Advances in Experimental Medicine and Biology*, *84*, Membrane Toxicity, 139–163.

Michael, B. D., Adams, G. E., Hewitt, H. B., Jones, W. B. G. and Watts, M. E., 1973. A post-effect of oxygen in irradiated bacteria: a sub-millisecond fast mixing study. *Radiation Research*, *54*, 239–251.

Ward, J. F., 1978. Radiation damage to DNA in aqueous solution: effects of radiosensitizers. *British Journal of Cancer*, *37*, Suppl. III, 42–45.

EFFECTS OF IONIZATION EQUILIBRIA ON THE RADIOSENSITIZING PROPERTIES OF NITROIMIDAZOLES

By E. D. Clarke, R. S. Jacobs, C. E. Smithen,* R. G. Wallace,† P. Wardman, M. E. Watts and M. Woodcock

*CRC Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN; *Roche Products Ltd., Welwyn Garden City, Herts. AL7 3AY; †School of Chemistry, Brunel University, Uxbridge, Middlesex UB8 3PH*

We have demonstrated previously that the efficiency of many different, uncharged nitroimidazoles in radiosensitizing hypoxic Chinese hamster cells *in vitro* is predominantly influenced by variations in redox properties and that other molecular properties, *e.g.* lipophilicity, are less important *in vitro*. We now report the behaviour of many new nitroimidazoles which carry acidic or basic groups in the side-chain(s) or ring substituents so that the molecule is partially ionized or protonated at physiological pH. Typical of the former are carboxylic acids or imidazoles with ring nitrogen unsubstituted; of the latter, ω-amino-alkyl bases. Some compounds of the latter type are more than an order of magnitude more efficient radiosensitizers (on a concentration basis) than misonidazole *in vitro*, although most are also more cytotoxic. Some acids exhibit unusual sensitizer enhancement ratio/concentration curves. The radiobiological data may be compared with the values of pK_a of the ionization equilibria; the variation in reduction potential with pH is also considered.

Reprints of these abstracts may be obtained from The Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6867).

SYNTHESIS AND EVALUATION OF HYPOXIC CELL SENSITIZERS FOR CLINICAL USE

By I. J. Stratford

Institute of Cancer Research, Sutton, Surrey SM2 5PX

Recently published work has shown a correlation between electron affinity and sensitizing efficiency for a range of different classes of compound including quinones, nitrobenzenes, nitrofurans, 2-nitro-imidazoles and 5-nitroimidazoles (Adams *et al.*, 1979). More recently, the radiobiology group at Sutton has synthesized and tested as radiosensitizers a series of 5-substituted-4-nitroimidazoles, compounds which have reduction potentials in the range −340 to −620 mV. These compounds are far more efficient sensitizers than would be suggested from their electron affinities. As much as a 100 fold lower concentration was required to give an enhancement ratio (ER) of 1.6 compared with what we would have expected from our previous correlation, *e.g.* NSC 38087 ($E^1_7 = -342$ mV) gives an ER of 1.6 at 2.6×10^{-6}M. The results suggest that mechanisms additional to electron affinity can operate in the radiation sensitization of hypoxic cells. Identification of these mechanisms should result in the synthesis of more active compounds which may then be useful clinically.

REFERENCE

Adams, G. E., Clarke, E. D., Flockhart, I. R., Jacobs, R. S., Sehmi, D. S., Stratford, I. J., Wardman, P., Watts, M. E., Parrick, J., Wallace, R. G., and Smithen, C. E., 1979. Structure-activity relationships in the development of hypoxic cell radiosensitizers I. Sensitization efficiency. *International Journal of Radiation Biology*, *35*, 133–150.

SURVIVAL AND TRANSMISSION OF SYMMETRICAL CHROMOSOMAL ABERRATIONS

By J. R. K. Savage

MRC Radiobiology Unit, Harwell, Didcot, OX11 0RD

Unlike asymmetrical (A) chromosomal aberrations, symmetrical (S) types do not normally give rise to acentric fragments nor pose mechanical separation problems at mitosis, and they are therefore the forms most likely to be transmitted to future cell generations.

Using chromosome banding techniques, most S-types can be scored with high efficiency, and evidence from both relative frequency and the distribution of pattern disruption points indicates that A and S are equally likely alternative modes of lesion interaction.

We have shown (Savage and Bigger, 1978) that S-types can be detected in fibroblasts many years after therapy in clinically normally skin taken from the irradiated area. The question arises: Is there any selection against S-types with time *in vivo*? Syrian hamster flank skin was sampled one day and six months after irradiation with 3 Gy of 250 kV X rays. Short-term fibroblast cultures were initiated under standardized conditions, and cells were fully scored after 15 days. Significant reductions in both S-types and deletions were found by six months. Distribution studies are consistent with a long-term *in vivo* repair mechanism.

Finally, breeding studies to follow the transmission of symmetrical translocations in Syrian hamsters have uncovered the fact that these animals can tolerate a considerable amount of chromosomal imbalance without phenotypic effect. The reason appears to lie in the very large amount of late-replicating chromatin in this species.

REFERENCE

Savage, J. R. K. and Bigger, T. R. L., 1978. Aberration distribution and chromosomally marked clones in X-irradiated skin. In *Mutagen-induced chromosome damage in man* (Edited by Evans, H. J. and Lloyd, D.), p. 155–169 (Edinburgh University Press).

SOME EFFECTS OF HYPERTHERMIA ON NORMAL TISSUES

By S. B. Field, Susan P. Hume and Marylin P. Law

MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

Hyperthermia causes at least two qualitatively different responses in normal tissues. More severe treatment results in a reaction which is different from that to ionizing radiations. Mild hyperthermia which does not cause detectable injury sensitizes tissues to radiation, the response being qualitatively similar to the tissue simply having received a greater dose of radiation. The thermal enhancement ratio (TER) can be derived and for both normal and neoplastic tissues it increases with increasing temperature or heating time. However, for heat and X rays given within a short time of each other the TER for some tumours is not higher than that for normal tissues so there is no obvious therapeutic advantage of treating in this way. Reasons why this might be so are given. Since direct heat damage is expected to be greater on tumour than on normal tissue, it may be therapeutically advantageous to use heat and radiation as separate modalities. This may be done by heating at least four hours after irradiation when the interaction between the two modalities has faded and only the direct component of heat damage will remain.

When repeated treatments are given, either of heat alone or in combination with X rays, prior hyperthermia is shown to render tissues temporarily less sensitive. For direct heat injury this induced resistance is a large effect both in skin and intestine. Its time course and extent are dependent on the first heat treatment, but resistance can be detected after treatment of as little as two minutes at 43.5°C. In general the induced resistance is lost within one week.

Prior heating does cause a small reduction in the TER when heat is given before irradiation, but it has no such effect if heat is given after irradiation. This is borne out by multifraction combined heat and radiation experiments in which the TER decreases with decreasing dose per fraction if heat is given before radiation, but not if the radiation is given first.

DOSE RATE EFFECTS IN AN IRRADIATED POST MITOTIC SYSTEM

R. W. Davies, A. J. Mill and J. V. Webb

Departments of Physics and Radiobiology, Medical College of St. Bartholomew's Hospital, London EC1M 6BQ

The effect of dose-rate on radiation-induced lifeshortening in *Drosophila melanogaster* has confirmed the presence of repair processes in this essentially post mitotic organism.

Adult flies were irradiated with single doses of 15 MeV electrons from a pulsed beam at dose rates from 0.5 Gy s^{-1} to 70 Gy s^{-1}. Lifeshortening was assessed by comparing the lifespan of irradiated flies with that of sham-irradiated control flies. Doses delivered at rates exceeding 10 G s^{-1} reduced relative lifespan to a greater extent than doses delivered at 0.5 G s^{-1}. There was no significant difference in response between flies irradiated at the lower dose rate with pulses of electrons and with continuous ^{60}Co gamma rays. The results were explained by the presence of repair processes which act during the time taken to deliver the dose at the lower rates.

The influence of hypoxia on these processes was investigated by irradiating groups of flies in air or nitrogen with electrons at high or low dose rate. The protective effect of hypoxia was confirmed for both high and low dose-rate irradiation and there was no evidence for inhibition of repair by this level of hypoxia.

RESPONSE OF AN *IN VIVO–IN VITRO* TUMOUR TO X RAYS AND CYTOTOXIC DRUGS: EFFECT OF TUMOUR DISAGGREGATION OF CELL SURVIVAL

By J. S. Rasey and N. J. Nelson

CRC Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, and Division of Radiation Oncology, University of Washington, Seattle, Wa, USA

Cell survival in EMT-6 tumours treated *in vivo* with cytotoxic agents can be assayed by colony-forming ability of cells plated *in vitro*. Tumours treated with single fractions of X rays, cyclophosphamide, or bleomycin were disaggregated with trypsin or a DNase-pronase-collagenase cocktail prior to plating of cells for determination of survival. The latter method was developed because it gives a 10–15 fold higher cell yield. The radiation cell-survival curves were identical for cells isolated by the two methods but cells prepared with trypsin appeared more sensitive to bleomycin and less sensitive to cyclophosphamide than did the cells prepared with the enzyme cocktail (Rasey and Nelson, 1979). Differences were sought in cells isolated by the two procedures. The radiation response data suggest that equally representative cell samples are isolated by the two disaggregation methods.

Both dissociation methods have similar effects in partially inhibiting DNA synthesis for the first few hours after cells are isolated. The fraction of newly plated cells able to incorporate ^{3}H-thymidine (11–16%) is reduced relative to the fraction which labels *in vivo* (25%). Patterns of potentially lethal damage repair are similar for cells isolated by the two techniques at various times after drug treatment.

The different effects of the two dissociation methods may be due to differential lysis of drug-damaged cells or to variable effects on drug entry and/or release. It is concluded that damage produced by cytotoxic drugs and enzyme-caused injury can interact to modify profoundly the tumour cell-survival curve for *in vitro* assay following *in vivo* treatment.

REFERENCE

Rasey, J. S. and Nelson, N. J., 1979. Effect of tumour disaggregation method on results of *in vivo* treatment and *in vitro* assay in the EMT-6 tumour. I. Comparison of response to X-rays, cyclophosphamide, and bleomycin. *In Vitro* (submitted).

RECOVERY FROM SUBLETHAL DAMAGE BY HYPOXIC TUMOUR CELLS *IN VIVO* AND *IN VITRO*

By N. J. McNally, K. C. George* and J. de Ronde

*CRC Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN and *Biological and Agricultural Division, Bhabha Atomic Research Centre, Trombay, India*

The ability of hypoxic tumour cells to recover from sublethal damage following irradiation *in vivo* and *in vitro* has been measured using a single mouse tumour system. The methods of assay were tumour growth delay, local tumour control and cell survival *in vitro* following treatment *in vivo* or *in vitro*. Tumours *in vivo* or cells *in vitro* rendered acutely hypoxic during irradiation were irradiated with either single doses or two doses 24 hours apart. Cells left *in situ* had a greater capacity for recovery than those either treated *in vivo* or *in vitro* and assayed *in vitro*. The results imply that *in vitro* assays may underestimate the ability of tumour cells left *in situ* to recover from sublethal damage. Tumours may not show a systematically reduced capacity for recovery relative to normal tissues.

RESPONSE TO SINGLE AND FRACTIONATED RADIATION OF JEJUNAL CRYPTS IN MICE TREATED WITH CYTOTOXIC DRUGS

By J. V. Moore

Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX

Using the intestinal crypt microcolony assay, the administration of graded doses of cytotoxic drug plus a test dose of radiation gives a first estimate of the response to drug of the crypt "stem" cells. The response to alkylating agents plus 10 Gy of γ rays was exponential, with no obvious initial shoulder (Moore, 1979). For vincristine (VCR) the surviving fraction (SF) of crypts reached a plateau at low doses of drug. However, the level of the plateau varied with the interval between modalities, SF decreasing as the interval was increased between 5 min and 10 h. It is suggested that this variation may have been caused by synchronization of cells surviving treatment so that at different times after VCR populations of different average D_q were being irradiated. The time-dependent variation persisted when both agents were given as four daily fractions so that the "overall" D_0 for γ rays alone was 8.81 Gy, for VCR-2h-γ D_0 was 4.82 Gy and for VCR-7h-γ D_0 was 3.01 Gy.

REFERENCE

Moore, J. V., 1979. Ablation of murine jejunal crypts by alkylating agents. *British Journal of Cancer, 39*, 175–181.

EFFECTS OF NEUTRONS ON NORMAL TISSUES AND TUMOURS

By S. Hornsey

MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

Two rationales for a therapeutic gain with neutrons were reviewed. The first is due to the reduction in OER with fast neutrons and the second due to variations in repair between low and high LET radiation for different tissues. The OER for different energy neutron beams was reviewed showing that from $E_d=16$ MeV(Be) to $E_p=160$ MeV(Be) the OER did not change significantly. Over the same energy range the RBE for skin and intestine fell by 60%.

It was suggested that the very small or zero slope of neutron isoeffect curves was due to the increasing contribution to damage from the heavy-recoil component of dose as the dose per fraction is reduced.

RBE data were reviewed and showed little firm evidence that RBE for late fibrosis was greater than for acute damage, although there is evidence that the RBE for radiation myelopathy is significantly higher than that for skin. Residual damage was higher after neutrons making retreatment after high LET hazardous.

RBE for tumour response to fractionated irradiation was very variable, showing that a therapeutic gain would be expected for some tumours but not all.

Book reviews

Diagnostic Radiography. A concise practical manual. By Glenda J. Bryan, pp.xii+398, illus., 3rd edn, 1979 (Churchill Livingstone, Edinburgh), £8·00.
ISBN 0-443-01923-1

The book is divided into three sections.

Part I, entitled "General Radiography", discusses principles involved in radiography, including chapters on the diagnostic use of radioisotopes and ultrasound. A chapter on computed tomography has also been added in this third edition.

Part II, "Regional Anatomy", divided into ten chapters, describes basic radiographic projections for each region of the body. Some of the possible supplementary views that are mentioned have been illustrated although no illustrations of basic projections are included. Some diagrams are given to aid description of patient positioning.

Part III, "Radiological Procedures", includes details of patient preparation, trolley settings, contrast agents, apparatus, radiographic technique and after-care of the patient for each examination described; some are illustrated.

The aim of the author "to provide a practical guide for the day-to-day work of an X-ray department" has, I think, been achieved. Possibly more radiographic illustrations might have been helpful but this volume would prove a useful handbook to both students of radiology and radiography. I feel it would be of most use in working areas for immediate reference but should not be used to replace the specialized textbooks already in common use.

J. L. MELLOR.

Encyclopedia of Medical Radiology. Vol. 9, Part 5a. *Roentgendiagnosis of the upper alimentary tract and air passages, the respiratory organs and the mediastinum.* By H. Behrend, H. Blaha, M. Loew, W. Schermuly and V. Schneider, pp. xii+737, 1978 (Springer-Verlag, K.G.), DM580/$319.
ISBN 3-540-08387-1

This volume deals with tuberculosis, sarcoid and lymphogranuloma of the lungs and with tumours of the chest wall. The list of references is formidable but there are very few from the 1970s. The illustrations are good but not even Springer-Verlag have managed to illustrate miliary tuberculosis. The book may well be the definitive radiological text on the diagnosis of tumours of the chest wall and tuberculosis of the lungs in all its varieties and combinations with other diseases. It will serve as a very good reference book for the practising radiologist but he will have to look somewhere else if he needs up-to-date information.

G. M. STEINER.

Transverse Anatomy of the Human Thorax, Abdomen and Pelvis. An Atlas of Anatomic, Radiologic, Computed Tomographic and Ultrasonic Correlation. By A. C. Wyman, T. L. Lawson, and L. R. Goodman, pp. xv+135, 1978 (Little, Brown and Co., Boston), $39.95
ISBN 0-316-96250-3

Axial anatomy has understandably assumed a new importance because of computed tomography and ultrasonography, resulting in a number of new books. Inevitably, these books will be largely pictorial, with illustrations relating CT and ultrasound sections to anatomical specimens, and, inevitably too, the many normal variations will be ignored.

Unfortunately, moreover, black-and-white photographs of axial body sections do not show anatomical details very clearly, if at all, and often the matched radiographs of the sections are more detailed.

Modern anatomical texts now show axial sections viewed from below to match corresponding CT and ultrasound prints, which is a great help for the uninitiated, but the mature student will need much more detailed information than is shown. However, the coloured photographic plates of body sections in the central section, though few in number, are extremely helpful, particularly in showing the relationship of the hepatic veins to portal veins.

There are, however, no over-riding features which would give this book preference over the many others that have recently appeared on the market.

L. KREEL.

Differentialdiagnose der akuten Lungeninfiltrate. By V. Otto Gsell, pp.ix+100 (incl. index), 1979 (Georg Thieme Verlag, Stuttgart), DM.59.
ISBN 3-13-1743-01-8

Dr. Gsell, who is a clinician, has aimed to produce a handy, inexpensive monograph on the differential diagnosis of acute lung infiltrates and has succeeded admirably by packing a lot of information into a well and clearly laid out text, only 100 pages long and measuring 9in. × 6in., in soft back. There are no radiographs. There is a very good index and a useful list of references. This little book goes a long way to providing a quick answer to such frequent questions as "does such and such a condition affect the lungs, and how?", and then indicates further reading. Practising radiologists and examination candidates will find this a very useful book.

G. M. STEINER.

Obituary

Dr. I. R. S. Gordon, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Dr. Ian Ronald Simson Gordon, who was Consultant Radiologist to the Bristol and Weston Health District (Teaching), died suddenly on June 12 whilst playing a game of tennis. He was 64 years old. Ian Gordon qualified in medicine from the London Hospital and Cambridge in 1939. He obtained the M.R.C.P. in 1942 and the M.D.(Cantab.) in 1944. He was medically unfit to serve with the Armed Forces during the Second World War; he worked during this period as a physician in Bath. In 1950 he decided that instead of seeking a career as a general physician he would turn to diagnostic radiology. He came to the teaching hospital in Bristol to train and he obtained the D.M.R.D. in 1952. His considerable aptitude for radiology was recognized early. He was appointed Consultant Radiologist to the then United Bristol Hospitals and Clinical Teacher in Radiodiagnosis to the University of Bristol in 1954. His interest in the problems of children led to his assuming responsibility for the radiodiagnostic departments of the Bristol Children's Hospital and the Bristol Maternity Hospital. From this beginning Ian Gordon became one of the foremost paediatric radiologists not only in the United Kingdom but in Europe as well. His erudition and contribution to diagnostic radiology were recognized by the Royal College of Radiologists by the award of the F.R.C.R. without examination in 1975. He was a founder member of the European Society of Paediatric Radiologists to which he made substantial contributions. He was also a founder member of the Radiologists' Group in the British Paediatric Association which met for the first time last year in York. He was one-time Secretary and later Chairman of the South-West Radiologists' Association and South-Western Branch of The British Institute of Radiology.

He was shy and retiring in nature and always unassuming. However, he expressed his opinions, whether radiological, administrative or social, with quiet firmness and he earned very deservedly the respect of all his colleagues. He was very much part of the Bristol Children's Hospital and he was Secretary and later Chairman of its Medical Staff Committee. Over the years he amassed a wealth of experience and knowledge of the radiology of children which he recorded in a book *Diagnostic Radiology in Paediatrics* published under co-authorship with Dr. F. G. M. Ross in 1977. This book has received much acclaim in the United Kingdom and abroad. He was a great "measurer"; his chapter on "Growth and Development as Demonstrated by Radiology" in this book is outstanding and it has received much praise. He had a great interest and knowledge of bone disease in children and the establishment of the Bristol Bone Dysplasia Registry owed much to his enthusiasm. He did not confine his activities to the Children's Hospital, but also did sessions at the Bristol Royal Infirmary and was responsible for the X-ray department at the Bristol Dental Hospital for many years.

He was a conscientious and painstaking teacher of radiologists, surgeons, physicians, medical students and radiographers, and held many weekly clinico-radiological conferences with them. For many years he was the Royal College of Radiologists' Tutor for the South-Western Region. He had two heart attacks, one in 1963, and another five years ago; these never seemed to dampen his enthusiasm or energies, a fact which amazed his colleagues. Dr. Gordon was held in much affection by the medical fraternity in Bristol who will miss his personality and expertise a great deal. He was always able to see the good in everyone and seldom had a harsh word for anyone. One of the many reasons that made him an outstanding paediatric radiologist was the fact that he was invariably able to gain the confidence of his child patients and this liaison with them enhanced substantially the quality of his radiological examinations, even in otherwise apparently unco-operative children.

He was ably, lovingly and considerately supported by his charming wife Diana and six children to whom our sympathy goes in their great loss. His colleagues are grateful for his life and his memory.

F. G. M. Ross.

Forthcoming events

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).

Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Radiation Biology for Part I F.R.C.R. (Radiotherapy and Oncology)

An intensive course in Radiation Biology will be held at the Paterson Laboratories from January 21–25, 1980, inclusive. It is primarily intended for radiotherapists in training but it is also open to other students of radiation biology and experimental oncology. Lectures and demonstrations will be given by the staff of the Paterson Laboratories.

Enquiries should be addressed to Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX.

Diagnostic Imaging USA

Peachtree Plaza, Atlanta, Georgia. January 28–29, 1980. Twenty prestigious speakers from around the world in a market-oriented conference. Send for programme from Robert S. First, Inc., 19A Avenue Marnix, 1050 Brussels, or telephone (02) 512 50 63.

Radiobiology Meetings

Forthcoming radiobiology work-in-progress meetings to be held by The British Institute of Radiology comprise a general meeting on February 15th, and one on "Biological effects of doses below 2Gy" on May 16th, 1980. Both meetings will be held in the Institute's Reid-Knox Hall, 32 Welbeck Street, London W1M 7PG. Titles of proffered papers for the February meeting should please be sent immediately to Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, W1M 7PG (01-935-6237).

Radiology in the 1980s

A seminar critically appraising the use of imaging techniques will be held in the Clinical Research Centre, Harrow, on February 28–29, 1980. Early registration is recommended as the number of participants will be limited. Details from Dr. G. de Lacey, Northwick Park Hospital, Watford Road, Harrow, Middx. HA1 3VT.

Whither Neuroradiology?

An evening meeting to be held on January 18, 1980, organized jointly with the Royal Society of Medicine (Section of Radiology), The British Institute of Radiology and The Royal College of Radiologists. Speakers will include Prof. I. Sherwood, Drs. I. F. Moseley, B. S. Worthington, I. G. Wylie and K. J. Zilkha.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01-935 6237).

Cell and Protein Labelling with Gamma Emitting Radionuclides for *In Vivo* Studies

A meeting to be held on February 13, 1980 organized by the Nuclear Medicine Committee of The British Institute of Radiology, at Middlesex Hospital Medical School, London.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01-935 6237).

Investigative Laparotomy in Hodgkins Disease

A joint meeting of The British Institute of Radiology, the Royal Society of Medicine (Section of Radiology) and The Royal College of Radiologists to be held on February 15, 1980, organized by and held at the Royal Society of Medicine, London.

Prostate Cancer

The Royal College of Radiologists will be holding its second multidisciplinary clinical oncology symposium on February 22–23, 1980 at 66 Portland Place, London W.1.

It is intended for senior registrars, consultants and research workers, and selected topics on the subject of prostate cancer will be reviewed by authoritative speakers from the United Kingdom. The registration fee is £25.

Full details from the Meetings Secretary, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG.

Third Annual Refresher Course

The Society of Computed Body Tomography will offer its Third Annual Refresher Course, March 2–6, 1980 at the Del Coronado Hotel, San Diego, California. The course will include an assessment of "state of the art", 2–5 second CT body scanners, dynamic CT scanning, new insights into thoracic and abdominal anatomy as seen with CT, and CT-guides interventional techniques. The relationship of CT to other imaging methods, including ultrasound, nuclear medicine and angiography will be emphasized. The faculty will include Drs. Alfidi, deWinter, Doppman, Evens, Glenn, Goldberg, Haaga, Harrel, Hattery, Kazam, Korobkin, Kreel, Sagel, Sample, Schellinger, Sheedy, Stanley, Stephens and Wittenberg. The fee is $250.

For further information write to Robert J. Stanley, M.D., Mallinckrodt Institute of Radiology, 510 South Kingshighway, St. Louis, MO 63110, USA.

5th International Congress of the International Radiation Protection Association

Will take place in Jerusalem, Israel, March 9–14, 1980.

The scientific programme of the Congress will cover all aspects of radiation protection with emphasis on its central theme: radiation protection—a systematic approach to safety.

An interesting programme has been planned including a commercial exhibition and pre- or post-congress workshops and professional tours.

Social events and a programme for accompanying persons have been organized.

For further information: The Secretariat, 5th International Congress of IRPA, PO Box 16271, Tel Aviv, Israel.

Spring Meeting, BIR/RCR/RSM

A joint Spring Meeting, organized by The Royal College of Radiologists, will be held in Southampton on March 28–29, 1980. Particulars from the General Secretary, The British Institute of Radiology, or from The Royal College of Radiologists.

Forthcoming events

International Congress on Death and Dying

This congress will be held March 31–April 2, 1980, at Imperial College of Science and Technology, London, SW7. Further details may be obtained from the Conference Office, 37a Maida Vale, London, W9.

BIR Annual Congress 1980 and Scientific Exhibition

The British Institute of Radiology Annual Congress will be held on April 17–18, 1980 at the Royal Free Hospital and will include the Sylvanus Thompson Memorial Lecture, presented by Sir Richard Doll and the Mackenzie Davidson Memorial Lecture by Prof. C. Kellershohn.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

Symposium on Spine and its Contents

EAR "Symposium Vertebrologicum" (Spine and its Contents) will be held from April 23–25, 1980 in Prague, Czechoslovakia.

The subjects of this symposium will be recent advances and experiences in:

(a) Equipments and investigative methods of spine and spinal cord.
(b) Radioanatomy and physiology of spine and spinal cord.
(c) Radiodiagnosis of pathological conditions.
(d) Interventive (diapeutic) radiodiagnostic methods.

Copies of the programme are available from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

BIR Annual General Meeting

This will be held on Thursday May 15 at 32 Welbeck Street, London W1M 7PG, at 7.15 p.m., to be followed by the Presidential Address, given by Dr. N. G. Trott, on "The exploding atom: radioactivity in radiology".

Cerebral Blood Flow and Metabolism

A joint BIR/BNMS session on this subject will be held on the afternoon of Wednesday July 2, at Imperial College, London SW7, during the Eighth Annual Meeting of the British Nuclear Medicine Society. Abstracts of papers to be submitted are invited: forms and further details from Mrs. Angela Taylor, BNMS Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP. Deadline is March 15.

Cambridge Meeting on Chest Disease

This residential meeting will be held on July 9–11, 1980 in King's College, Cambridge. It should appeal to radiologists with an interest in chest disease, and chest physicians. The number of delegates will be limited and early application is advised.

Details from: Dr. C. D. R. Flower, Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge.

European Society for Radiation Biology

The 15th meeting of this Society will be held from August 25–29, 1980, at the Medical Faculty of the Erasmus University, Rotterdam, Netherlands.

Further information can be obtained from the Secretary of the Meeting, Dr. J. J. Broerse, Radiobiological Institute TNO, P.O. Box 5815, 2280 HV Rijswijk, Netherlands.

6th IAEA Symposium on Medical Radionuclide Imaging

This symposium, of interest to medical physicists and nuclear medicine physicians, will take place in Heidelberg, Federal Republic of Germany, from September 1–5, 1980.

Topics to be covered will include mathematics and physics of imaging; advances in instrumentation and techniques for imaging, display, and data processing; new radiopharmaceuticals; quality control; clinical applications; comparison of radionuclide imaging with other imaging modalities.

Further information regarding participation and/or submission of papers can be obtained from national atomic energy authorities or from International Atomic Energy Agency, P.O. Box 100, A–1400 Vienna, Austria. The deadline for receipt of abstracts, through official channels, is March 29, 1980.

European Symposium on Lung Cancer (EAR)

The symposium, organized by the Greek Radiological Society under the auspices of the European Association of Radiology will be held September 7–13, 1980 at Chalkidiki, Greece.

For further information contact the Secretariate, Department of Radiology, Areteion Hospital, 76 Vass. Sofias, Athens, Greece.

Measurement Standards in Respect of both Ionizing and Non-ionizing Radiation Hazards

An all day meeting with the National Physical Laboratory and The British Institute of Radiology is to be held on May 14, 1980 at the NPL, Teddington, Middlesex.

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Further information from: Secretariat ICR-81, Ave. Winston Churchill 234B-Box 16, B-1180 Brussels, Belgium.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

Instructions to authors

Please keep manuscripts brief and concise and include only those illustrations essential to an understanding of the text.

Much time and correspondence will be saved if authors pay careful attention to these detailed instructions.

Material published in The British Journal of Radiology includes full papers, case reports, technical and instrumental notes, short communications, letters to the editor and invited articles. Communications should ordinarily be addressed to the Honorary Editors, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Communications from North America, Continental Europe, Australasia or South Africa should preferably be submitted to the most appropriate of the following Associate Editors:

Dr. P. Armstrong, M.B., B.S., F.R.C.R., D.M.R.D., Department of Radiology, School of Medicine, University of Virginia, Charlottesville, Virginia 22901, USA (for diagnostic papers).

Prof. M. Cohen, Department of Physics, Montreal General Hospital, 1650 Cedar Avenue, Montreal, H39 1A4, Canada (for non-diagnostic papers).

Prof. B. J. Cremin, F.R.A.C.R., F.R.C.R., Department of Radiology, Groote Schuur Hospital, Observatory 7925, Cape Town, South Africa.

Dr. H. A. Luke, F.R.C.R., F.R.A.C.R., The Alfred Hospital, Prahran, 3181, Victoria, Australia (for diagnostic papers).

Dr. G. P. G. Sim, M.B., F.R.C.R., M.R.C.A., X-ray Department, Wellington Hospital, Wellington, New Zealand.

R. W. Stanford, Esq., M.A., F.Inst.P., Department of Medical Physics, Royal Perth Hospital, Perth, Western Australia (for non-diagnostic papers).

Prof. D. M. Taylor, Institute for Genetics and for Toxicology of Fissile Materials, Kernforschungszentrum, Postfach 3640, D-75, Karlsruhe J, Germany.

The acceptance of a paper for publication in The British Journal of Radiology is at the discretion of the Editors and is subject to the understanding that the material contained in the paper has not already been published and is not intended for publication elsewhere.

The copyright of all publications resides with The British Institute of Radiology.

The Editors take no responsibility for the return of MSS, prints, etc. submitted for publication.

MANUSCRIPT. The manuscript should be typewritten in English on one side of the paper only with double spacing and margins of at least 25 mm on both sides and at the top. The top copy must be submitted together with one duplicate. The address given in the title should be that of the department(s) or hospital(s) at which the work was carried out. If any author has subsequently moved to a new address, this should be given as a footnote. Degrees and diplomas of authors should be given but not more than three for each author. Tables (numbered I, II, etc.) should be given on separate sheets, and each should have a short descriptive title. Legends for illustrations, including diagrams and graphs, should be set out on a separate sheet, and denoted Fig. 1, 2, etc. The initial letter of trade or proprietary names should be a capital. Mathematical expressions should be set out very clearly.

UNITS, SYMBOLS AND ABBREVIATIONS

Authors should use the *International System of Units (SI)* (B.S.I., 1970; WHO, 1975). The publication *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (Royal Society of Medicine, 1977) is thoughtful and critical on this subject; authors are strongly recommended to follow the detailed suggestions in this guide and to note particularly the comments made on the choice of units. From Volume 53 (starting January 1980) units of radiation should be given in SI with the old units in parenthesis, thus 1 Sv (100 rem), 200 cGy (rad), 1 MBq (27 μCi). Some explanation and a table of conversions appeared in an Editorial, Vol. 52, page 1, 1979.

DIAGRAMS AND GRAPHS. Diagrams and graphs, including numerals and lettering, should be clearly drawn in black ink for photographic reproduction to a width of 76 mm (exceptionally 156 mm). Good quality photographic prints or the original art work should be supplied. Care should be taken that details such as numbering and experimental points remain legible after photographic reduction. Computer print-outs are seldom satisfactory. The figure number, author's name and title of article should be pencilled lightly on the back of each illustration.

Authors of physics papers will find advice on drawing diagrams, particularly electrical circuits, in *Notes for Authors* issued by the Institute of Physics and the Physical Society in 1976.

RADIOGRAPHS. Unmounted prints not larger than whole plate, 216 × 152 mm, and not smaller than half plate should be supplied with MSS; if the prints are not of sufficiently high standard for reproduction purposes the author will be required to submit the original radiographs and to defray the cost of making prints. Tracings of sections of prints are acceptable when necessary for additional clarification. Hospital illustrators and photographers are usually familiar with the style of drawing or print which will give the best reproduction.

COLOUR. Drawings or photographs in colour are very expensive and are acceptable only if the author is prepared to pay the additional cost of block-making and printing.

REFERENCES. The Harvard system is used. In the text these should consist of the names of authors and the year of publication. When there are more than two authors only the first followed by *et al.* should be used. In the bibliography references will be given *in full* and will include the title of the paper and the full name of the journal or other publication in which the article cited appeared. Both first and last page numbers are required. The references must be arranged in alphabetical order, in the following form:

Examples

Brownell, G. L., Aronow, S. and Hine, G. J., 1976. Radioisotope scanning. In *Instrumentation in Nuclear Medicine*, Ed. G. J. Hine, Vol. 1, pp. 381–428 (Academic Press, New York).

Watson, A., Russell, J. G. B. and Torrance, G. B., 1970. Hepatic blood flow and Biligrafin excretion during intravenous cholangiography. *British Journal of Radiology*, *43*, 248–250.

ABSTRACTS. Papers (other than case reports and technical notes) should be accompanied by an abstract. This abstract is not part of the paper, but is intended to convey the content of the paper, to draw attention to all new information and to the main conclusions, and should be intelligible in itself without reference to the paper. An abstract should not normally exceed 200 words.

CORRESPONDENCE. Letters for publication in the correspondence section of the journal must be confined to matters of interest to readers of this journal.

SHORT COMMUNICATIONS. These are reports of initial studies in new areas and comments which are too speculative or provocative for a normal paper. They should be kept as short as possible and must on no account exceed two pages of the journal. They will be published with the minimum delay.

REPRINTS. Twenty-five reprints of each paper are supplied free. Additional copies may be purchased. Reprints of correspondence items will not be supplied unless specifically requested.

SUPPLEMENTS AND REPORTS. Examples of material considered for publication as Supplements or in the Report Series are special monographs which are too long for publication within the journal, or detailed reports of certain meetings.

REFERENCES

British Standard 3763, 1976. *The International System of Units (SI)*, British Standards Institution, London (£4·50).

Institute of Physics, 47 Belgrave Square, London SW1, 1979. *Notes for Authors.*

The Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE, 1977. *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (£2).

University of Leeds
in association with
The Royal College of Radiologists

THE LEEDS GASTROENTEROLOGY COURSE FOR RADIOLOGISTS

will be held at
St. James's University Hospital
Leeds
Monday, 19 May to Friday Noon, 23 May 1980

The Course is designed mainly for Consultants and Senior Registrars who wish to sub-specialize in gastroenterology. It will have a sizeable clinical content and will emphasize special procedures.

The fee for the Course is £70·00 which includes lunches and morning and afternoon refreshments.

Residential accommodation can be arranged if required at a central hotel.

Early application is advised.

Full details together with programme and application form can be obtained from Mr. Frank Moran, Senior Administrative Assistant, Postgraduate Dean's Office, Littlewood Hall, Leeds General Infirmary, Leeds LS1 3EX.

The Charitable Infirmary
Jervis Street and St. Laurence's Hospital

CONSULTANT RADIOLOGIST

Applications are invited from qualified medical practitioners for the above post which includes a commitment of eight sessions per week at The Charitable Infirmary, Jervis Street and one session at St. Laurence's Hospital.

Applicants must possess the following qualifications:

(A) (i) The possession of the Fellowship of The Faculty of Radiology of The Royal College of Surgeons in Ireland or a qualification in Radiology at least equivalent thereto;

Or

(ii) The possession of a recognised diploma in Medical Radiological Diagnosis awarded before May, 1966 or a qualification in Radiology awarded before May, 1966 at least equivalent thereto.

(B) (i) In the case of persons who possess the qualifications at (i) above, the specialisation on a full-time basis, in the practice of Radiology for at least five years;

Or

(ii) In the case of persons who possess the qualifications at (ii) above, the specialisation on a full-time basis, in the practice of Radiology since acquiring such diploma.

Particulars of appointment may be obtained from the Secretary/Manager, Jervis Street Hospital, Dublin 1, to whom curricula vitae (10 copies) should be sent so as to reach him not later than 12.00 noon Thursday, January 31, 1980.

Guidelines for the Preparation of Radiopharmaceuticals in Hospitals
Revised 1979 Edition

Special Report No. 11

A Report of a Working Party

Numerous types of diagnostic agents labelled with radio-nuclides are now in routine use for the investigation *in vivo* of human disease. Many of these radiodiagnostic agents contain radio-nuclides of short half-life and for this and other reasons it is necessary to carry out their preparation in hospitals. Little official or other guidance concerning the basic procedures required for the safe preparation of these radiopharmaceuticals has, however, been available. For this reason, following a Seminar on 'Laboratory Facilities and Working Procedures for the Hospital Preparation of Radiopharmaceuticals' held at the Royal Marsden Hospital, Sutton, in October 1974, a working party was set up to prepare some guidelines on this subject. This document comprises the report of this working party; it is concerned not with individual recipes, but with basic principles and procedures. The Report should prove helpful to many of those concerned with the preparation and use of radiopharmaceuticals, and it is expected to provoke useful comment and discussion, especially on the extent to which the procedures set down conform to the requirements of the Medicines Act (1968).

In revising the present report it has not been considered necessary to revise any of the original recommendations. However, the opportunity has been taken to amend certain sections to take account of the changes in United Kingdom legislation consequent on the implementation of Article 5(a) of the European Communities Directive (Euratom, 1976) on basic safety standards for health protection against the dangers of ionizing radiation.

Additional references have also been provided, and minor changes made, where necessary to bring the text up-to-date.

Published by The British Institute of Radiology
32 Welbeck Street, London W1M 7PG
Price £2·50

VOL 53 NO 625 JANUARY 1980

The British Journal of Radiology

Contents

Ultrasonic scanning in suspected ectopic pregnancy. 1
J. F. Pedersen

The measurement of effective photon energy and "linearity" in computerized tomography. 5
D. R. White and R. D. Speller

The isocentric fast neutron therapy facility at Edinburgh. 12
D. E. Bonnett, J. R. Williams and C. J. Parnell

Late functional changes in the vasculature of the rat brain after local X-irradiation. 21
H. F. Moustafa and J. W. Hopewell

Technical notes. 26
Target angle and inferential kilovoltage measurement.
H. E. Crooks
A new ophthalmic ultrasonic B-scanner.
J. S. Paton, M. B. D. Cooke and G. R. Sutherland
A broad band microwave applicator for heating tumours.
S. Szwarnowski, R. J. Sheppard, E. H. Grant and N. M. Bleehen
A technique for producing localized measurable hyperthermia in superficial rat tumours using ultra-high frequency currents.
P. B. Dunscombe and B. M. Backhouse

Case reports. 38
Combined endoscopic and percutaneous trans-cystic approach to a retained common duct stone.
R. R. Mason and P. B. Cotton
De novo development of teeth in a teratoma.
Z. J. Ounjian, R. L. Mani and J. R. Mani

Correspondence. 42
Results of treatment of cancer of the cervix at Addenbrooke's Hospital, Cambridge, 1946–70.
Mary Mitchell, J. S. Mitchell and J. L. Haybittle
Dosage in high-energy electron therapy.
R. D. Hunter
Dose rates to staff in the event of failure of beam-control mechanism in cobalt-60 units.
C. Binks
Misonidazole also radiosensitizes some normal tissue.
G. Arcangeli, C. Nervi and F. Mauro
Traumatic para-mediastinal air cysts.
E. Ravin

Proceedings of The British Institute of Radiology (Preview of papers for the International Congress, Japan) April 1979. 46

Obituary: Dr. I. R. S. Gordon 50

Forthcoming events 51

Instructions to authors 53

Book reviews
1979 Year book of diagnostic radiology 4
Newer radiogases in practice 20
Atlas of nuclear medicine. 4. Bone 37
Computed tomography of abdominal abnormalities 37
Recent advances in radiology and medical imaging 41
Fundamentals of abdominal sonography 41
Diagnostic radiography 49
Encyclopedia of medical radiology 49
Transverse anatomy of the human thorax, abdomen and pelvis 49
Differentialdiagnose der akuten Lungeninfiltrate 49

Printed in Great Britain by Lund Humphries
London and Bradford
Published by The British Institute of Radiology
32 Welbeck Street, London, W1M 7PG

ISSN 0007-1285
14725

14.9.82

Volume 54 Number 63
January 198

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis
Radiation oncology
Nuclear medicine
Ultrasound
Radiobiology
Radiophysics
Radiation protection
and related disciplines

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C), F.R.C.R.
N. E. GILLIES, B.SC., PH.D.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C. CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance in sterling. Single copies: £6·00. Second class postage paid at New York. Mailing agents: N.Y. Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York, N.Y. 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01–935 6237 and 01–935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

APPEAL

A permanent home for British radiology

The Appeal Committee

Sir Jan Lewando, CBE (*Chairman*)
Professor G. H. du Boulay (*Appeal Co-Ordinator*)
Mr. L. F. Barr Smith
Dr. Julian Bloom
Sir Richard Doll, OBE, FRS
Mr. Kevin Hughes, OBE
Professor L. F. Lamerton
Sir Thomas Lodge
Dr. J. F. Loutit, CBE, FRS
Professor W. V. Mayneord, CBE, FRS
Professor J. H. Middlemiss, CMG
The Lord Penney, OM, KBE, FRS
Sir Edward E. Pochin, CBE
Sir John Read
Mr. C. F. E. Shakerley
Professor Sir David Smithers
Professor R. E. Steiner, CBE
Dr. Herman D. Suit
Dame Janet Vaughan, FRS
Professor Sir Brian Windeyer
The Lord Zuckerman, OM, KCB, FRS

The President of the Institute and Appeal Executive Committee members

Funds are still needed for the new permanent home for The British Institute of Radiology at 36 Portland Place, London W1, next door to the Royal College of Radiologists

Donations and ideas to:
Appeal Co-Ordinator, 32 Welbeck Street, London W1M 7PG (01–486 5084)

polyfoam®

ANSAFONE SERVICE
operates 5pm-9am and at weekends

unique padding permits passage of X-rays without showing on the plate

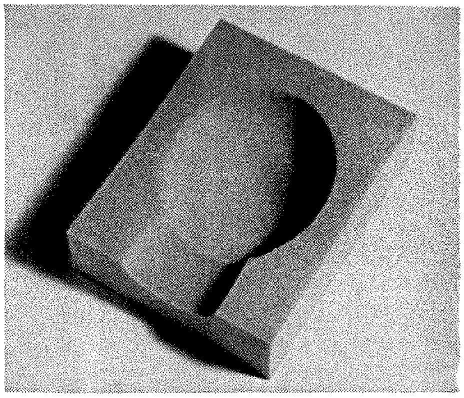
RADIOLOGISTS

helped to design this Polyfoam position block
ADULT SIZE BLOCK 202, 10″×8″×3″
CHILD'S SIZE BLOCK 303, 7″×6″×2″

These blocks as illustrated are cut from a single block of Polyfoam and provide a comfortable non-slip positioning block which lets the patient relax more easily.

POLYFOAM BLOCKS 202 & 303

For more information please write or telephone:



HINDERS-LESLIES LIMITED
Higham Hill Road · London · E17 6EJ
Telephone: 01-531 7172 (10 lines) plus Ansafone

progress
through
research

S&N Member of the SMITH & NEPHEW Group of Companies

University of London

ROYAL POSTGRADUATE MEDICAL SCHOOL

COURSE IN FAST NEUTRON THERAPY

8–12 June 1981

A Specialist Short Course (in two parts) organised by the Royal Postgraduate Medical School and the Medical Research Council Cyclotron Unit, Hammersmith Hospital.

Part I: Physics and Radiobiology: 8 and 9 June.

Part II: Clinical Methods and Results: 10—12 June.
This course will cover all major aspects of Fast Neutron Therapy and will be divided into two parts to accommodate the needs of both scientists and clinicians. Participants may attend either or both parts of the course.

Part I Will deal in detail with the physics and radiobiology relevant to fast neutron therapy and will include demonstrations of the adjustable collimators, activation analyses, neutrograms and other appropriate techniques. Dosimetry and properties of higher energy neutron beams will be discussed.

Part II Will consist of indications for and results of neutron therapy, together with descriptions of the techniques specially developed for neutron treatments. Results of completed controlled clinical trials will be discussed and current international trials will be reviewed. Patients will be available for examination and early and late effects on normal and malignant tissues will be related to dose, technique and time after treatment. Specialists in ophthalmology, dermatology and gastroenterology will compare details of neutron effects with those of photons. Radiobiologists will be present for discussion of RBE's of various tissues. The use of the E-cat scanner in studying physiological effects of tumours and radiation will be described.

Because of the emphasis on the examination of patients by participants on the course numbers for Part II will be limited to 16.

Course organisers: Dr Mary Catterall and Dr D K Bewley

Fees (inc catering):	Part I	£40 for home and EEC participants £150 for overseas participants
	Part II	£60 for home and EEC participants £200 for overseas participants
	Whole Course	£75 for home and EEC participants £300 for overseas participants

Application forms from: School Office (SSC)
Royal Postgraduate Medical School
Hammersmith Hospital
Du Cane Road

Tel: 01-743 2030 ext 351 London W12 0HS

Closing date for applications: 20 March 1981

Now there's a fully integrated, fully automatic film handling and processing system that makes daylight radiography a total daylight process. From loading the film magazine right through to producing the finished radiograph, the Trimatic Daylight Loading System from 3M brings daylight radiography truly out of the shade.

But it has to be experienced to be believed.

For detailed information just ring Alan Budge on Bracknell (0344) 58458 or write to him at X-Ray Products, 3M United Kingdom Ltd, FREEPOST, Bracknell, Berkshire RG12 1BR.

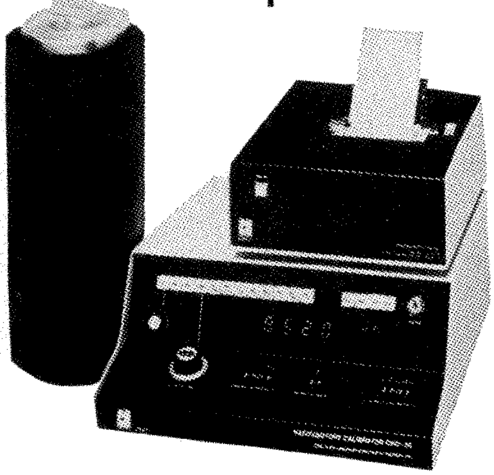
THE TRIMATIC DAYLIGHT SYSTEM: IT DOES WHAT OTHER DAYLIGHT SYSTEMS CAN'T.

3M and Trimatic are trade marks.

3M

When reliability counts

You can count on Radioisotope Calibrators from Capintec



The Capintec range adds a new dimension to Radioisotope Calibration.

The CRC-30 is a complete system and features include:—

- **Fully detailed patient dose print-out.**
- **Built in Radiochemical purity analyser for high quality imaging.**
- **Computes and prints post-calibrated volumes.**
- **Computes and records target to non-target ratio.**
- **Reduces operator radiation exposure.**

internuclear

U.K. distributors for: Atomic Development Corp.,
Atomic Products Corp.,
Capintec Inc., Medicor, Medi-Physics Inc.,
Sinmed Benelux b.v., Veenstra Instrumentum b.v.

Internuclear Limited, 18 Bath Road,
Swindon, Wiltshire, SN1 4BA.
Telephone: (0793) 30579 and 38888. Telex: 449493.

THE ONTARIO CANCER FOUNDATION
TORONTO-BAYVIEW CLINIC

Chief Physicist

A Chief Physicist is required for this new cancer centre which is associated with Sunnybrook Medical Centre and The University of Toronto. Construction of the out-patient and radiation treatment facility will be completed in October 1981. Four megavoltage machines, including two 25 MEV linear accelerators, will be installed.

The Centre will treat 2500 new patients a year and will have a major research orientation. The initial staff will include six Radiation Oncologists, six Medical Oncologists, and three Physicists.

The Chief Physicist will head the Division of Clinical Physics and lead an active research programme.

Interested individuals should send a curriculum vitae and the names of three referees to:

Dr. R. D. T. Jenkin, Director, The Ontario Cancer Foundation, Toronto-Bayview Clinic, 2075 Bayview Avenue, Toronto, Ontario, M4N 3M5.

DIAGNOSTIC RADIOLOGIST

CERTIFIED

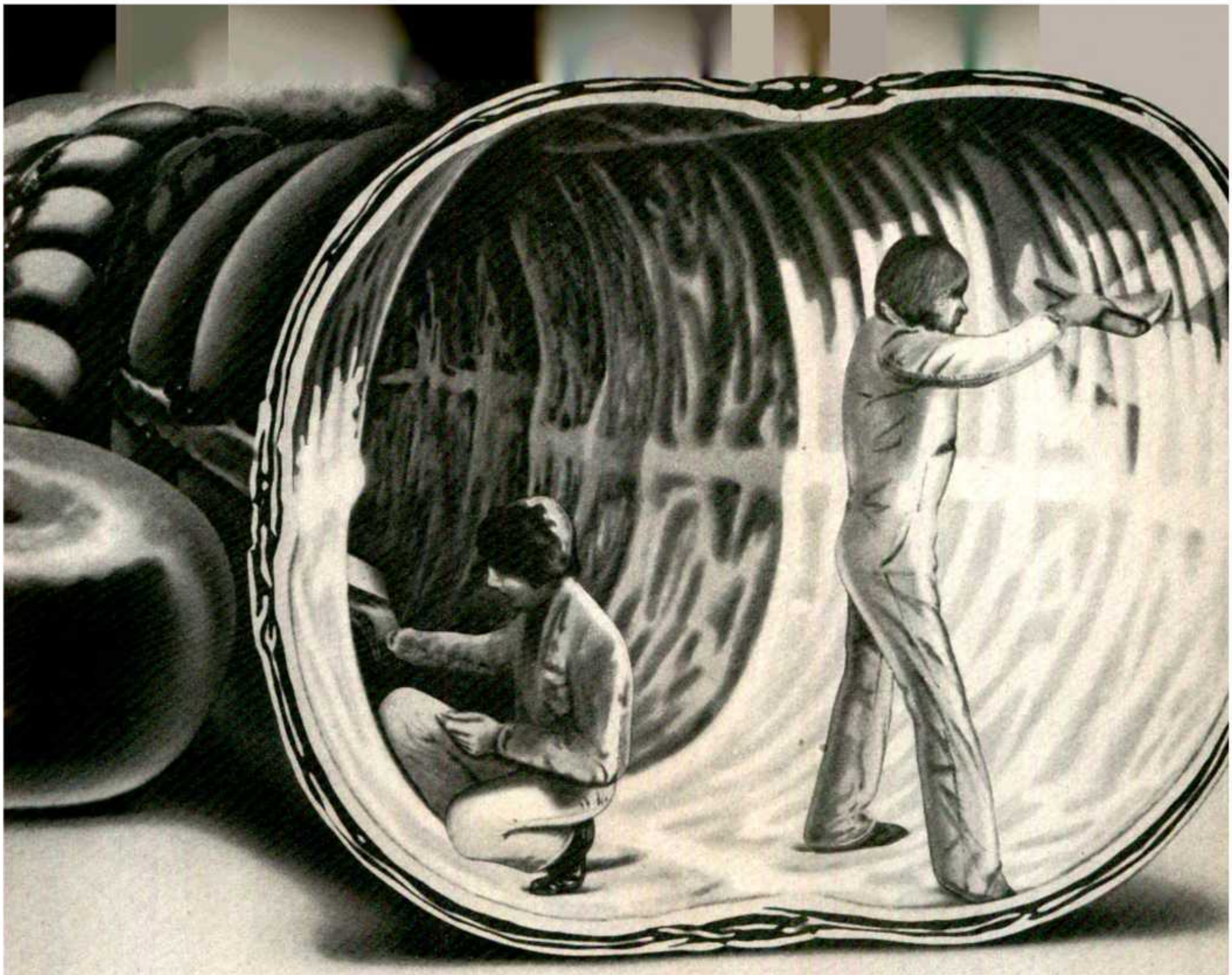
CANADA

Required for a 571 bed hospital complex serving a community of 250,000, located across the river from Detroit, Michigan, U.S.A. a community of 2 million; a well established cultural and educational centre – excellent recreational facilities. Present Radiologist retiring.

Services include a wide range of Radiology, Angiography and special procedures. Ultra Sound equipment is on order and plans are in progress for the development of the new ultra sound facility.

Remuneration by Fee for Service – Ontario Hospital Insurance Plan.

Apply to: **Mr. G. E. Pickard, Executive Director, Windsor Western Hospital Centre Inc., 1453 Prince Road, Windsor, Ontario, Canada N9C 3Z4**



baritop ensures smooth and even coating of the GI tract

The high density, low viscosity and ultra-fine particle size of Baritop allows optimum visualisation of the areae gastricae and the innominate grooves. Baritop consistently gives excellent resolution.

Baritop 100 is a ready made suspension supplied in a ring-pull can for easy use. If you prefer a higher density use Baritop G powder.

Baritop makes the most of your double contrast technique.

Concept Pharmaceuticals Ltd.,
Russell House, 59-61 High Street, Rickmansworth WD3 1EZ
Tel: Rickmansworth (092 37) 79388/9/0 Telex: 925794

baritop

for those who seek perfection

A Practical Introduction to Cranial CT

A. R. Valentine, P. Pullicino and E. Bannan

This book is designed to introduce doctors and technical personnel to the application of CT in neurological and neurosurgical diagnosis. It should become essential reading as CT becomes even more widely available and accepted. It will be particularly relevant to radiologists, and also to neurological clinicians, both medical and surgical and most useful for those encountering the technique for the first time. But established practitioners will also benefit much from an up-to-date synopsis as well as reiteration of some technical and anatomical details.

The text is extensively illustrated throughout.
ISBN 0-433-33602-1   160 pp   £8·00

Also available:

C. Metreweli: Practical Abdominal Ultrasound

This book fulfils a need for anyone learning how to use diagnostic ultrasound in obstetrics and in general abdominal investigation.
ISBN 0-433-21311-6   160 pp   £15·50

Coming in February:

Clark's Positioning in Radiography

Vol. 2 The extensively revised 10th Edition by Louis Kreel.
ISBN 0-433-188332   448 pp   £22·50

Thomas Jefferson University Hospital

The Division of Diagnostic Ultrasound at Thomas Jefferson University Hospital, under the direction of Barry B. Goldberg, M.D., offers ongoing diagnostic ultrasound courses for physicians and sonographers. Basic and advanced courses include the abdomen and pelvis, obstetrics and gynecology, echocardiography, physics and instrumentation, real time and cross sectional anatomy. The facility includes invited speakers and members of the full time staff (which consists of four physicians and nine sonographers). In addition to the extensive lecture program, the participants benefit from case review material, exposure to the diversified equipment used in ten examination rooms, and the availability of an extensive videotape and reference library. Participants may choose from one or more weekly courses, a month or more Preceptorship Program, or an individual customized program. The weekly courses are limited to twenty participants and early enrollment is advised. Fees vary with the program. All programs have Category I Credit.

For further information and course dates, contact:
Barry B. Goldberg, M.D., Course Director, or Kathy Bonner, Education Secretary, Division of Diagnostic Ultrasound, 1015 Walnut Street, 5th Floor, Philadelphia, PA 19107, USA. Phone: 215–928–8533.

PRM 80

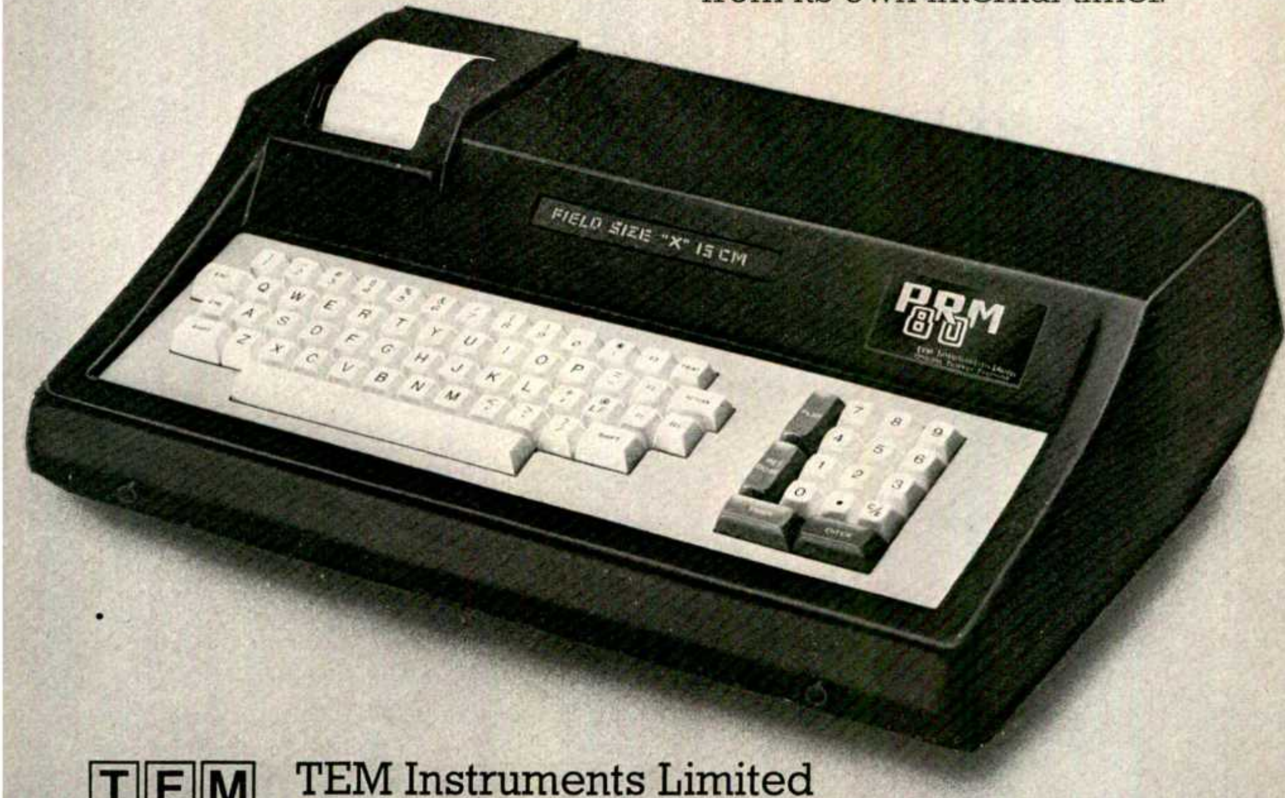
The T.E.M. programmed radiotherapy microcomputer has been developed to handle the everyday task of accurately calculating a patient's treatment dose and/or time.

From these entries:
- Field sizes
- S.S.D.
- Attentuation Factors
- Depth of Tumour
- Prescribed Dose Etc.

The PRM 80 gives:
- Treatment Time
- Set Dose
- Skin Dose.

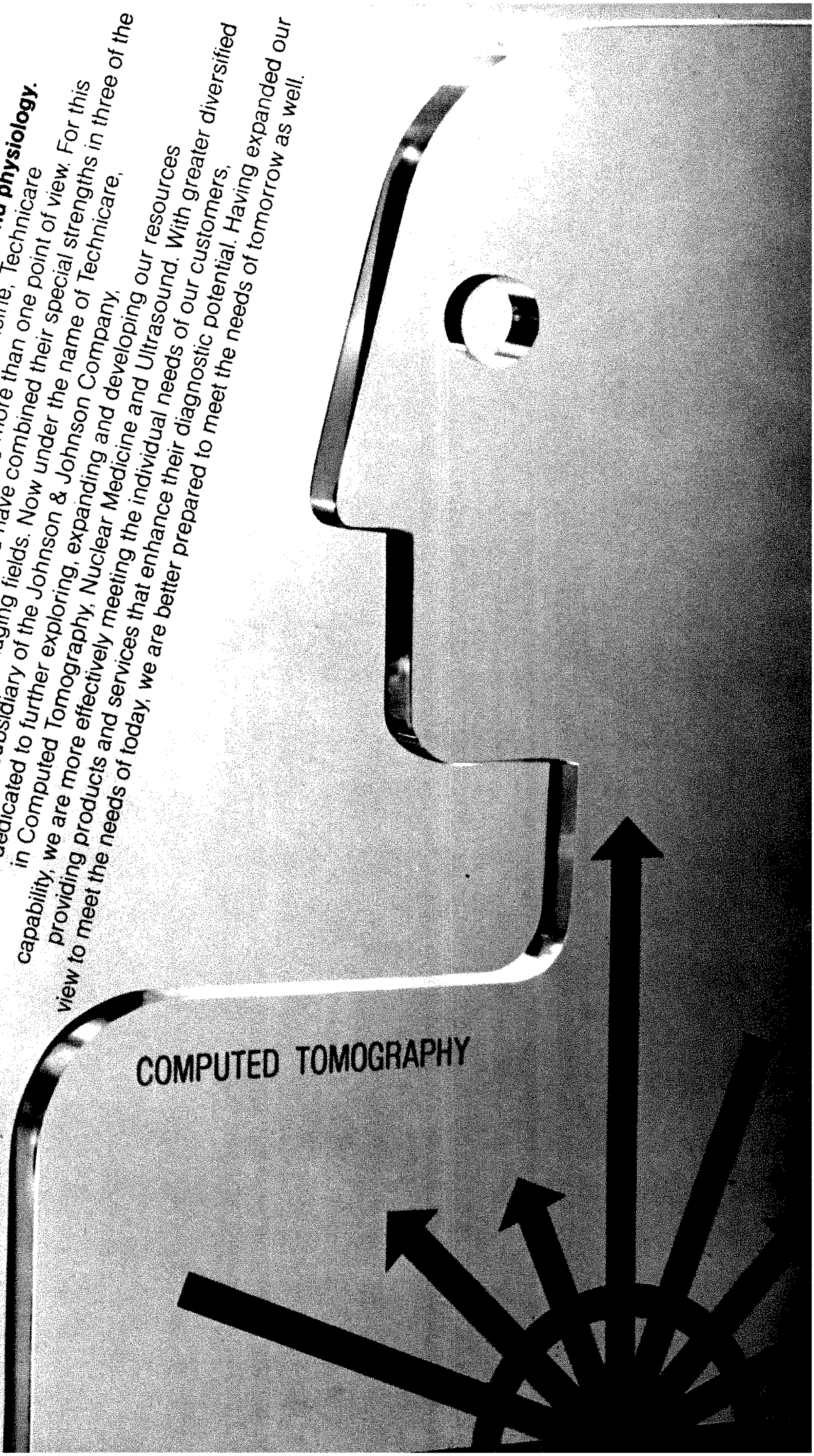
Capable of calculating opposed field and off-axis data, the PRM 80 also has an optional facility giving the total number of treatments, cumulative dose and the ret dose.

The PRM 80 prints out all this data, including the actual treatment time which is recorded from its own internal timer.



TEM

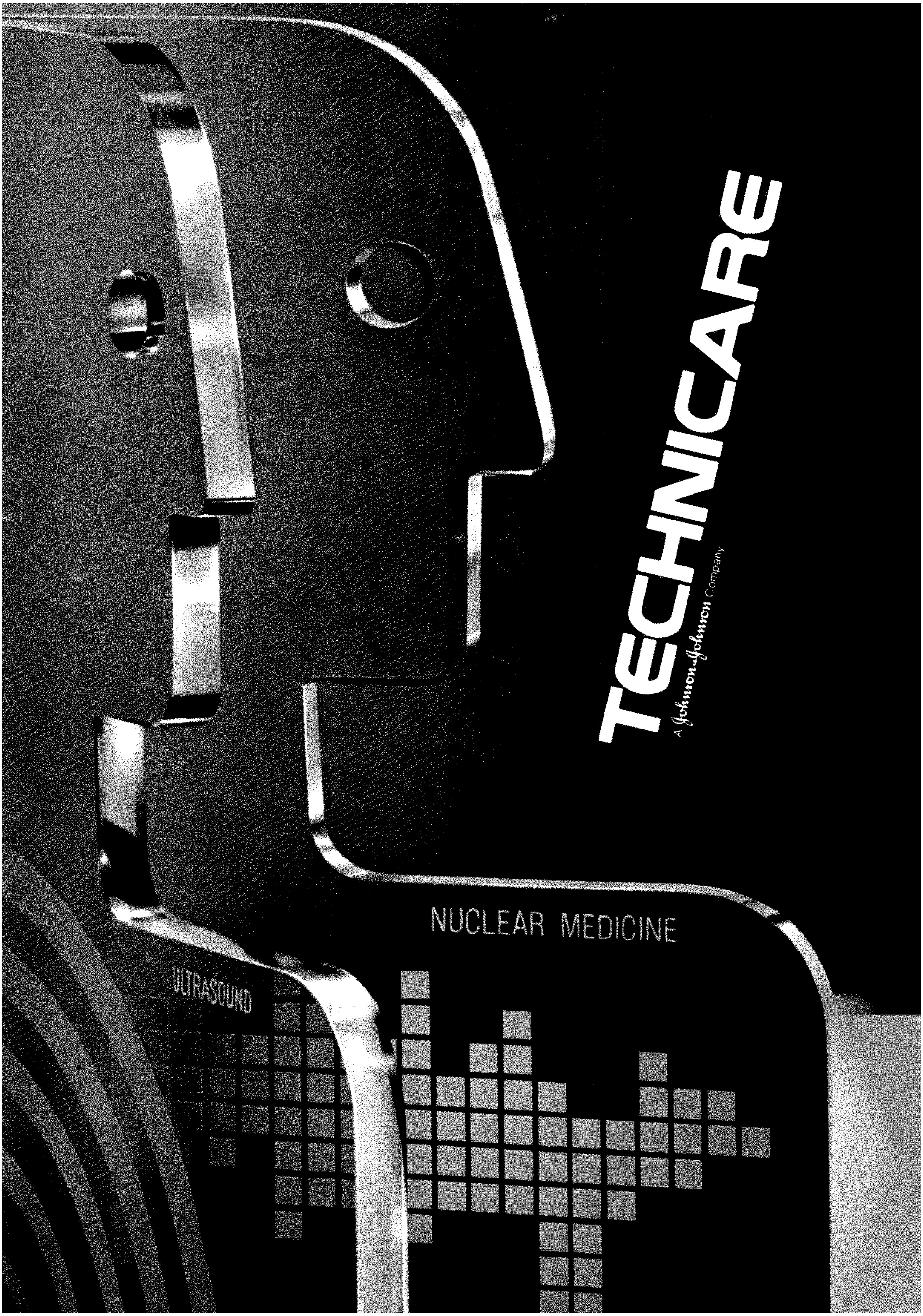
TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England
Tel: 0293 31244 Telex: 87397, Grams: TESTMENT CRAWLEY



Together . . . we provide a clearer view of human anatomy and physiology.

As specialists in the field of diagnostic medicine, Technicare recognizes the advantage to having more than one point of view. For this reason Ohio Nuclear and Unirad have combined their special strengths in three of the most important diagnostic imaging fields. Now under the name of Technicare, and as a subsidiary of the Johnson & Johnson Company, we are dedicated to further exploring, expanding and developing our resources in Computed Tomography, Nuclear Medicine and Ultrasound. With greater diversified capability, we are more effectively meeting the individual needs of our customers, providing products and services that enhance their diagnostic potential. Having expanded our view to meet the needs of today, we are better prepared to meet the needs of tomorrow as well.

Technicare, 29100 Aurora Road, Solon, Ohio 44139 U.S.A.; Telephone: (216) 248-1800; Telex: 810-427-2694.
World Offices: Amsterdam, Athens, Auckland, Beirut, Bologna, Bombay, Brussels, Buenos Aires, Caracas, Delhi, Hong Kong, Lima, Madras, Madrid, Melbourne, Mexico City, Milan, Montreal, Osaka, Paris, Quito, Rome, Rugby, Santiago, Sao Paulo, Seoul, Stockholm, Sydney, Taiwan, Thessaloniki, Tokyo, Vancouver, Vienna, Wiesbaden, Zurich.


TECHNICARE
A Johnson & Johnson Company
NUCLEAR MEDICINE
ULTRASOUND

FACULTY POSITIONS OPEN

Colleges of Medicine & Medical Sciences
Department of Radiology

King Faisal University

Dammam, Saudi Arabia

TEACHING APPOINTMENTS

The expanding Colleges of Medicine & Medical Sciences invite applications for their Radiology Department.

Candidates should have a minimum of 2 years teaching or practical experience.

Language of instruction is English.

Salaries are highly competitive and negotiable, comparable to other Saudi Arabia Universities.

Benefits:

Free furnished accommodation. Local transport allowance. Educational assistance for up to 4 children. Airfare to and from Saudi Arabia once a year for husband, wife and 2 children, plus a 60-day paid holiday. Interviews will be held in the United Kingdom and the United States. Please send 3 copies of complete curriculum vitae and names, addresses and telephone numbers of 3 references to:

Dr. Tawfik Tamimi, M.B., Ch.B., Ph.D.
Dean, Colleges of Medicine & Medical Sciences
King Faisal University

at the appropriate address below:

PO Box 2
Sunbury-on-Thames
Middlesex
TW16 5JP
England

c/o Saudi Arabian Educational Mission
2425 West Loop South
Houston
Texas 77027
USA

The King Faisal University Teaching Hospital opens shortly.

High dose-rate after-loading in the treatment of cancer of the uterus

Edited by Thelma D. Bates and Roger J. Berry

British Journal of Radiology Special Report 17

For more than fifty years intracavitary irradiation has formed a major part of the treatment of cancer of the cervix and corpus uteri. In recent years high dose-rate remote after-loading devices have been developed which have removed all radiation hazards to medical and ancillary staff and other patients, but until now the question "Are the clinical results achieved by high dose-rate after-loading intracavitary treatment of carcinoma of the cervix and corpus uteri at least as good as those achievable by conventional low dose-rate intracavitary techniques?" had not been answered by adequate clinical experience. At a meeting held at The Middlesex Hospital Medical School, London from 10–12 April 1978, 86 participants and observers from 36 Hospital Centres in 15 countries gathered to discuss relevant physics and radiobiology studies and to pool their clinical experience in the use of high dose-rate after-loading devices. This volume presents brief versions of their 33 contributed papers and a distillation of the lively discussion which took place. Although the conclusions reached were necessarily cautious, lest future results not reflect those already achieved, those so far with remote high dose-rate after-loading appear to be in no way inferior to the results of traditional methods. In fact there are indications that high-dose fractionated intracavitary therapy may be associated with a lower incidence of normal tissue complications for a comparable level of achievement of tumour local control in cancer of the cervix and corpus uteri.

High dose-rate remote after-loading devices have the ability to treat very large numbers of patients, and have a particularly valuable contribution to make in the treatment of these distressingly common cancers in developing countries. This volume provides a comprehensive view of clinical and radiobiological experience for those centres acquiring or considering high dose-rate after-loading equipment.

Orders to:
Price **£15**
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
(01–935 6237) or through your bookseller.
ISSN: 0306–2120
ISBN: 0–905749–07–3

SHIMADZU HD150B SERIES
THREE-PHASE HIGH POWER X-RAY GENERATOR WITH SINGLE PHASE COMPACTNESS AND EASE OF OPERATION

Three-phase x-ray high tension units have come to replace single-phase type gradually because of the feasibility of the large current and exposure of ultra short time that enable high quality roentgenogram to be taken.

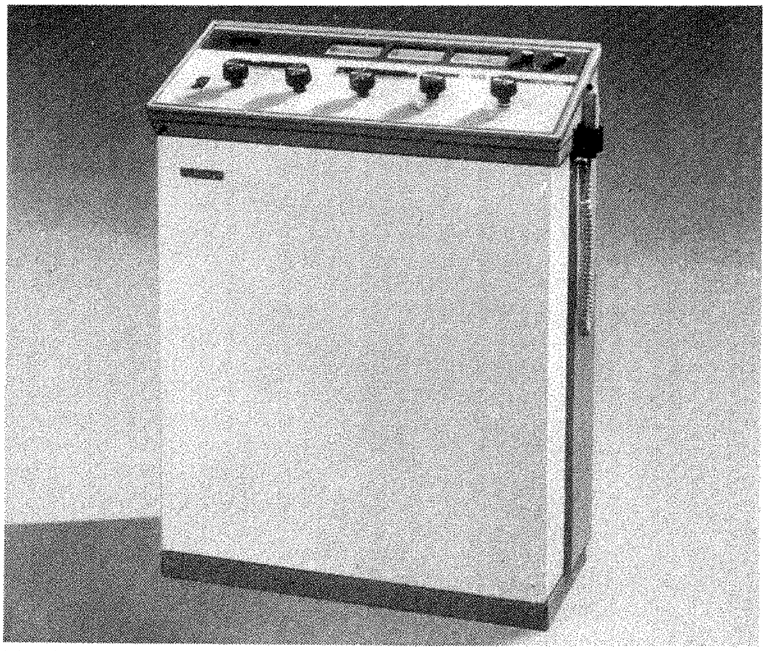
The HD150B series finds wide range of applications from small current radiography made possible by a fine-focus x-ray tube along with development of high quality films, intensifying screen etc. to large current radiography such as angiocardiography.

INCORPORATED FEATURES

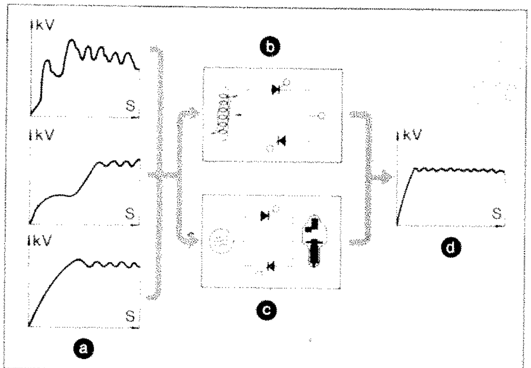
- **Magnetic presetting and quick response function highly effective for short time exposure**

The magnetic presetting to prevent saturation of magnetic flux and the quick response mechanism to prevent generation of excessive voltage, which is Shimadzu's unique control system, achieves clean three-phase wave form of quick rise and good reproducibility, enabling highly reliable radiograph to be taken in short-time radiography.

- **Solid-state control of x-ray exposure**
- **Solid-state tube voltage control**
- **Fluoroscopy timer**
- **Independent setting of tube voltage**
- **Load factor indication and overload protection**
- **Control unit made into a console type compact design**



MAGNETIC PRESETTING AND QUICK RESPONSE SYSTEM



ⓐ Three-phase wave-form of bad rise caused by saturation of magnetic flux and excessive voltage.

ⓑ Magnetic presetting system to prevent saturation of magnetic flux.

ⓒ Quick response mechanism to prevent generation of excessive voltage.

ⓓ The clean three-phase waveform of quick rise and good reproducibility achieved by the magnetic presetting and the quick response mechanism.

ⓔ "TIME GAIN" realized by the adoption of the load factor meter.

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku,
Tokyo 160, Japan. Phone: Tokyo 03-346-5641
Overseas Telex No.0232-3291 SHMDT J Cable Address SHIMADZU TOKYO
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone 01-902-6098 ENGLAND

St. James's University Hospital Leeds

F.R.C.R. Preparation Course

Monday 2 to Friday 6 March 1981

St. James's University Hospital in association with the University of Leeds is to present a Course designed to prepare candidates for the F.R.C.R. Examination. The course will give practice in answering multiple choice questions, long written questions and short written questions. There will be film recognition examinations and oral confrontations. As far as is possible all these will be held under examination conditions.

In addition, review lectures of subjects felt to be poorly handled by previous candidates will be given in Chest, C.N.S, Spine, Bone, Urinary Tract, Ultrasound, C.T. Scanning, Paediatrics and Nuclear Medicine. The course will be hard work. Course organisers: Dr. W. P. Butt and Dr. L. Kreel

Course Fee £100 inclusive of lunches and refreshments.

Residential accommodation can be arranged if required.

Full details together with programme and application form can be obtained from Mr. Frank Moran, Senior Administrative Assistant, Postgraduate Dean's Office, Littlewood Hall, Leeds General Infirmary, Leeds LS1 3EX.

Diagnostic Radiologist

Diagnostic Radiologist wanted, with fellowship or eligible, to join radiological group in Edmonton, Alberta, Canada. Hospital and office practice. Applicant should have training in special procedures and or ultrasound. Please reply to Box No. 23

WANTED

DIAGNOSTIC RADIOLOGIST

required for group in large western Canadian city. Training in ultrasound, mammography and Nuclear Medicine an asset. Private clinic practice and hospital affiliation. Please reply to Box No. 7, British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

RADIATION PROTECTION of the PATIENT

A Manual of Good Practice

Edited by : Walter A. Langmead

Part I. — Diagnostic Radiology

Price £2.95

This Manual is concerned with the radiation protection of patients undergoing diagnostic examinations or treatment with ionising radiations. It examines the responsibilities of the many individuals — general practitioners, clinicians, radiologists, radiographers and physicists — whose special fields of knowledge together contribute to the radiation safety of the patient, and it proffers advice to each in turn as to the preferred procedures to minimise the patient's radiation dose without reducing the level of diagnostic achievement or the efficacy of treatment.

The Manual is to be published in three Parts, dealing respectively with radiology, nuclear medicine and radiotherapy. PART I. — DIAGNOSTIC RADIOLOGY, covers the X-ray examination from the initial request to the final report. The scientific and technical factors which enable the clinical objectives to be attained with minimal dose to the patient are also reviewed. Two Appendices give recommendations respectively for certain specialised X-ray examinations, and for a departmental guide to radiographic procedures.

The benefits of medical diagnosis and treatment with radiation are large, and the potential radiation hazards arising therefrom are comparatively minor in most cases. Nevertheless, the safety of the patient is paramount and this results from good teamwork and attention to detail, as outlined in this Manual.

Prepared by Panels of the British Radiological Protection Association; and published by the British Institute of Radiology.

Orders to BIR Publications, 32 Welbeck Street, London W1M 7PG (01-935 6867)

Toshiba portable real time scanner SAL-20A

Linear phased array real time scanner with compound scan equivalent image quality, specifically designed for obstetrics, gynaecology and internal medicine.
New, patented type of transducer.
Standard delivery includes electronic calipers.

Toshiba

TOSHIBA

Oldelft

This product is handled by:
Oldelft Deltronix bv
Fruitweg 9, 2525 KE Den Haag,
Holland, Tel. (070) 88 89 63.
Telex 32195.

België/Belgique 2100 Deurne,
Twee Gezusterslaan 34, Tel. (031) 24 93 05.
Deutschland D 6300 Giessen/Lahn,
Postfach 5420, Tel. (0641) 4 10 49.
England Croydon CRO 1JN,
16 Barclay Road, Tel. (01) 68 11 17 1.

España Madrid 16, Uruguay 13,
Tel. (01) 259 1698.
France 91403 Orsay, B.P. 86,
Tel. (01) 9075900.
Italia Via della Vasca Navale 84,
Tel. (06) 5584311.

Schweiz 8618 Oetwill am See,
Zelglistrasse 5, Tel. (01) 929 13 18.
Sverige 17206 Sundbyberg 6, Postbox 670,
Tel. (08) 98 38 95.

Carcinogenesis and Radiation Risks: a Biomathematical Reconnaissance

by W. V. Mayneord, C.B.E., D.Sc., F.R.S. and R. H. Clarke, Ph.D.

with foreword by Sir Eric Pochin, M.D.

British Journal of Radiology Supplement No. 12, 1975; reprinted 1979.

The first printing of this refreshingly original monograph by Professor Mayneord and Dr. Clarke was sold out. In view of the increasing interest in the topics dealt with by the authors, the work was reprinted. It explores some of the fundamental problems that arise when one attempts to predict the biological effects of a given dose of radiation. The authors point out that, in attempting an estimate of biological effect, for example carcinogenesis, it is frequently assumed that the risk is simply proportional to the dose received, although biological experiment often reveals a much more complex relation between effect and dose. They examine some of the consequences of taking such complex relationships into account in assessing "risk" on the basis of "dose" and propose a formula relating the risk to a whole population of cells from a rare event, such as the "transformation" of a single cell or group of cells. The parameters of the basic formula can be varied to meet particular assumptions regarding the distribution of dose in tissue and of response to dose. Using this formula, analyses are made of many different types of problem, including those presented by "point sources". It is emphasized throughout that the derivation of probabilities is not merely an exercise in mathematical physics but also involves cytology, genetics, immunology and hormone physiology, as well as studies of viral and chemical carcinogenesis. However, the method of analysis used leads to a clearer definition of the problems that have to be studied in attempting to produce more logical estimates of the risks from radiation, and the quantities of significance in designing experimental investigations.

The monograph represents a detailed development of ideas presented by Professor Mayneord in his Mackenzie Davidson Memorial Lecture of 1968 on "Radiation Carcinogenesis" and workers in the fields of radiobiology, experimental carcinogenesis and health physics will gain valuable insights from this study.

Orders to: Price **£6·50**

Publications Department, The British Institute of Radiology,
32 Welbeck Street, London, W1M 7PG (01–935–6237) or your bookseller.

1981, *British Journal of Radiology*, *54*, 1–7
VOLUME 54 NUMBER 637 JANUARY 1981

The British Journal of Radiology

Less common stress fractures in the foot

By K. O. A. Meurman, M.D.
Department of Radiology, First Central Military Hospital, Helsinki, Finland

(*Received June 1980*)

ABSTRACT

In a series of 827 stress fractures in soldiers, 15 were found in the first metatarsal, representing 11% of all stress fractures in the metatarsals. All were in the proximal end of the bone. Eight fractures were found in the fourth and four in the fifth metatarsal. In the cuneiform bones three fractures were found, and one in the talus. One fracture was revealed in the lateral sesamoid of the hallux and one in the peroneal bone. Ten patients had stress fractures in other bones too. The radiological appearance and the corresponding stress mechanisms are discussed.

The incidence of stress fractures varies in different statistics but tibial, metatarsal and calcaneal fractures represent almost 80% of them (Darby, 1967; Wilson and Katz, 1969; Rückert and Brinkmann, 1975; Geslien *et al.*, 1976). In the metatarsals, stress fractures (march fractures) occur mostly in the second and third (MT II, MT III), and are less common in the first, fourth and fifth (MT I, MT IV, MT V). Table I shows the incidence of stress fractures in the second group by some authors. Stress fractures are extremely rare in the tarsal bones, except in the calcaneum; some solitary reports have been published for the cuneiform bones (Maseritz, 1936; Childress, 1943; Meurman and Elfving, 1980). Stress fractures are also very rare in the tarsal navicular and in the talus (Devas, 1975; Meurman, 1980). Occasionally stress fractures have been found in the sesamoid bones of the foot (Golding, 1960; Devas, 1975; Orava *et al.*, 1978).

TABLE I

INCIDENCE OF STRESS FRACTURES IN THE I, IV AND V METATARSALS AS GIVEN IN THE LITERATURE

Author(s)	Total number of stress fractures	Stress fractures of		
		MT I	MT IV	MT V
Tobold, 1903	1500 (suspected fractures)	1	not given	
Nion, 1903	330 (MT only)	0	17	6
Kirchner, 1905	not given	1	not given	2
Asal, 1936	153 (MT only)	1	not given	1
Bernstein and Stone, 1944	307 (MT only)	3	not given	1*
Bernstein *et al.*, 1946	724 (MT only)	2	25	4
DeVan and Carlton, 1954	145 (MT only)	0	10	3
Kroening and Shelton, 1963	not given	1	1*	1*
Gilbert and Johnson, 1966	over 2000	6	not given	
Maurer, 1970	169	3	5	1
Orava *et al.*, 1978	142 (athletes)	0	4	2

*Stress fractures also of MT II in the same foot.

For the present investigation, the radiographic material of the Central Military Hospital, Helsinki, Finland, was studied for stress fractures in these less common sites.

PATIENTS AND METHODS

A total of 827 stress fractures had been recorded in 700 patients (1971–1980). Almost all the patients were military recruits. The history, symptoms and signs were recorded. Tomography was occasionally needed in addition to conventional radiographs. A complementary study with isotope scanning was carried out with 50 patients.

RESULTS

In the foot 176 fractures of the calcaneum were found in 133 patients (43 of them were bilateral), and 140 fractures of the metatarsals in 135 patients (five bilateral). Of these there were 58 stress fractures in MT II (two bilaterals) and 55 in MT III (one bilateral). In the less common sites, 33 stress fractures were found in 30 patients, as shown in Table II. These represent 4% of the total material and 10% of all stress fractures in the foot.

Two patients had bilateral fractures of MT I. Another also had a stress fracture of the medial cuneiform. Ten patients had stress fractures in other

TABLE II

Distribution of the less common stress fractures of foot in the present material

I metatarsal	15
IV metatarsal	8
V metatarsal	4
Medial cuneiform	2[*]
Lateral cuneiform	1[1]
Talus	1[1]
Lateral sesamoid of hallux	1
Peroneal bone	1
total	33

[*] The other previously reported by the author.
[1] Previously reported by the author.

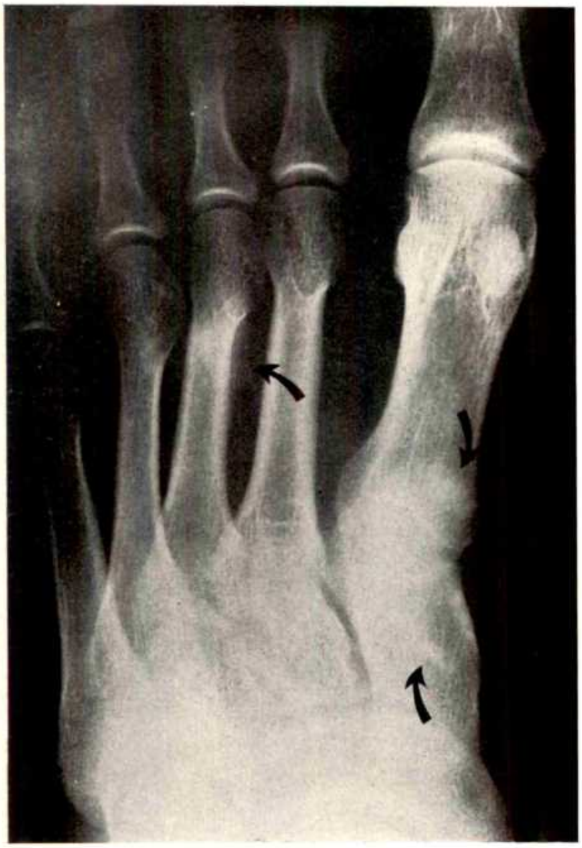


Fig. 1.

Three stress fractures in the same foot. Internal callus in the base of MT I and in the medial cuneiform. Periosteal callus in the neck of MT III. The patient had also stress fracture of MT I in the other foot.

TABLE III

Stress fractures in other bones

Site of the less common stress fracture	Other bones involved	Time of appearance of the other fractures
I metatarsal, left	calcaneum, left	later
I metatarsal, right	calcaneum, left	simultaneous
I metatarsal, left	pubic arch, right femoral shaft, right	simultaneous simultaneous
I metatarsal, bilateral	medial tibial condyle, right	simultaneous
I metatarsal, bilateral	III metatarsal, left I cuneiform, left	simultaneous simultaneous
IV metatarsal, right	III metatarsal,left tibial shaft, bilateral	simultaneous earlier
IV metatarsal, left	II and III metatarsal, left	simultaneous
V metatarsal, right Talus, right	tibial shaft, right calcaneum, left	simultaneous earlier
Medial cuneiform, right	medial tibial condyle, right	later

bones, too (Fig. 1). These are shown in more detail in Table III. One patient (MT V) had a recurrence in the same site six months later.

The patient with fracture of the peroneal bone was an officer. All the others were recruits. Sixteen of them were white-collar workers and 13 were labourers. Two of the patients with fracture of MT V and one with fracture of MT IV were sportsmen, all others were non-athletes. The patients represented various military personnel, but the basic training programme had been the same for them all. Two patients (MT I and MT V) had slight lumbar scoliosis and two (MT I) had low-arched feet.

Symptoms and Signs

In all recruits the symptoms began with pain during basic military training. In 14 patients the pain began during the cold period when the terrain is frozen, in two of them (MT I and MT IV) after skiing. The pain increased with continued stress and mostly caused limping. In the two athletes with fracture of MT V, the pain appeared during strenuous running, in one of them during the 12-minute test (Cooper, 1968). In one patient with fracture of MT V no specific stress could be implicated.

The patient with fracture of the sesamoid of the hallux had a two-week history of stress pain. The patient with the peroneal bone fracture had a feeling of progressive pain during jogging over a period of several months.

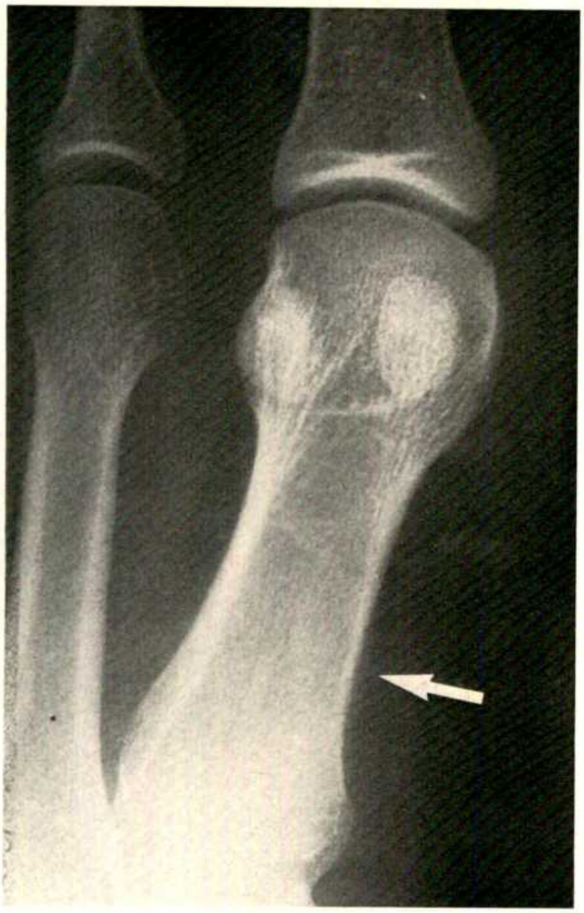


FIG. 2.
A delicate periosteal callus in the base of MT I three weeks after the onset of pain.

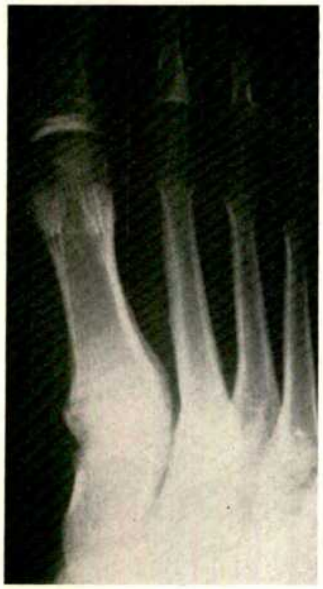


FIG. 3.
A transverse fissure across the bone in the base of the MT I. Intramedullary and periosteal callus.

On clinical examination, local tenderness, and often local swelling, were found at the sites of the fractures, mostly on the dorsal side of the foot. The lateral sesamoid of the hallux was extremely tender, as was the peroneal bone on the inner border of the foot.

RADIOGRAPHIC FINDINGS

In all the fractures of MT I the radiographic changes were on the proximal border of the bone. Transverse intramedullary callus was found on the medial side in five patients (Fig. 1). In some of these the callus was best visualized in the "wrong" oblique position, and was further confirmed by tomography. In one patient, a slight periosteal callus formation on the medial proximal border of the diaphysis was seen (Fig. 2). In all other patients both internal and periosteal callus were seen. A transverse fissure across the bone was found in three patients. No dislocation was seen (Fig. 3).

The fractures of MT IV were in the middle or distal part of the diaphysis showing cortical break and periosteal callus formation. One patient had a complete fracture across the shaft with some displacement.

In two patients with fracture of MT V, a cortical break was seen laterally in the proximal part. The third patient showed slight periosteal callus at the first examination and one month later the callus was seen surrounding the shaft of the bone like a tube. No fissure was found (Fig. 4). In the fourth patient an oblique cortical fissure with very slight periosteal callus was found in the shaft (Fig. 5).

The fractures of the talus and of the cuneiform bones appeared as sclerotic bands in the bone (Fig. 1).

In the lateral sesamoid of the hallux a small avulsion of the proximal corner of the bone was seen (Fig. 6). The radiograph of the peroneal bone showed several fragments with diastasis between the main fragments which had irregular borders (Fig. 7).

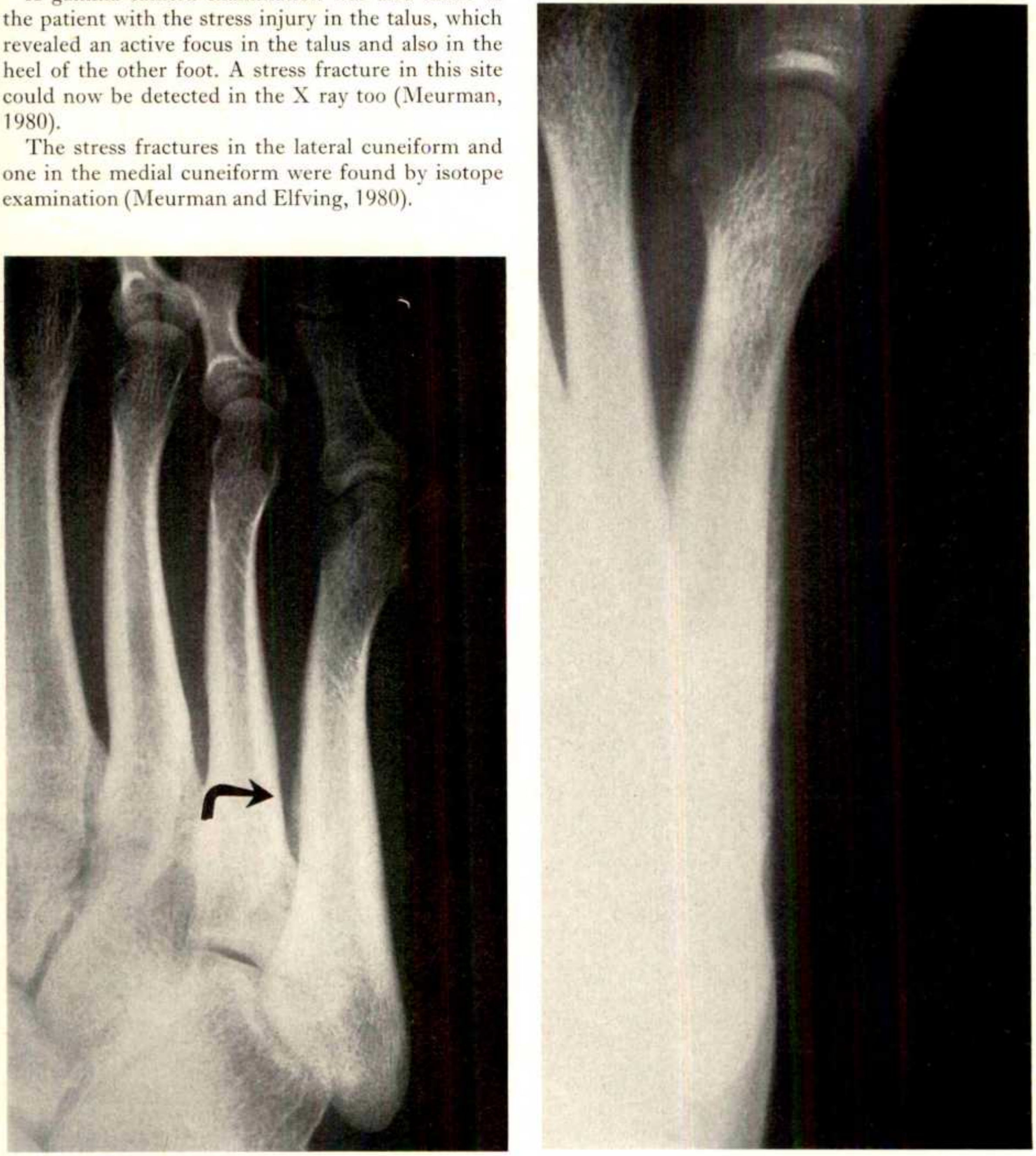
SPECIAL FEATURES

One patient had pain in the right knee (previous meniscectomy), and on the dorsal side to the left foot. The X ray revealed a stress fracture of the medial tibial condyle, but not in the foot. An isotope scan was taken and revealed increased activity in the tibial condyle and also in the proximal ends of both MT I. An X-ray re-examination now showed callus formation, indicating stress fracture in these sites too.

A gamma-camera examination was also made of the patient with the stress injury in the talus, which revealed an active focus in the talus and also in the heel of the other foot. A stress fracture in this site could now be detected in the X ray too (Meurman, 1980).

The stress fractures in the lateral cuneiform and one in the medial cuneiform were found by isotope examination (Meurman and Elfving, 1980).

In one patient in whom a gamma-camera investigation showed sites of increased activity in the bases of both MT I, the radiographs revealed stress fracture only on the left.



A Fig. 4. B

(A) Slight periosteal callus in the MT V two weeks after the onset of pain.

(B) The same foot one month later. Tube-like callus surrounds the shaft. No fractures in the other metatarsals.

DISCUSSION

Radiologically, stress fractures are classified into two main types. The compression fracture appears as internal transverse callus, while the distraction fracture appears as periosteal callus indicating a cortical fissure or break (Devas, 1975; Savoca, 1971).

In the present material, both types were found in MT I, although in most patients a mixed image was seen with both intraosseous and periosteal callus. This was especially true in the cases with transverse fissures (Fig. 3). The instability of the fracture may be an additional factor in the production of periosteal callus.

According to Devas (1975), the fractures of MT I are compression fractures since this bone takes a large proportion of the body weight. Apparently a breaking mechanism in the thick base of this bone seems unlikely. Devas also reported that stress

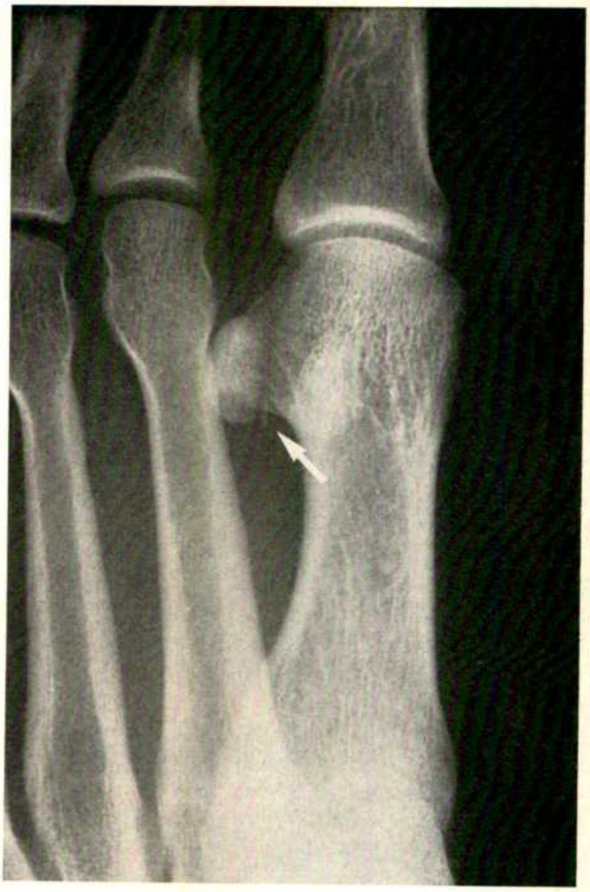


FIG. 6.

A fracture of avulsion type of the proximal corner of the lateral sesamoid of the hallux. A two weeks history of stress pain.

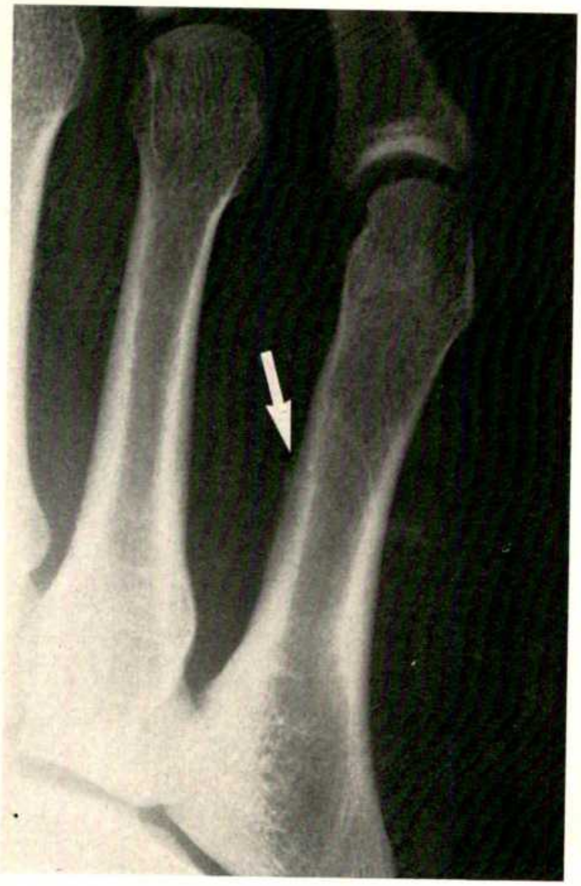


FIG. 5.

An oblique cortical fissure with slight periosteal callus in the middle part of the shaft of MT V. No fractures in the other metatarsals.

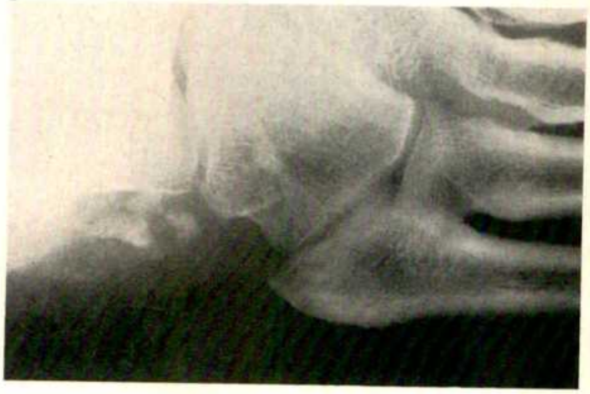


FIG. 7.

The peroneal bone is separated into several fragments with diastasis between the main fragments. Pain during jogging for several months. Local tenderness.

UNIVERSITY COLLEGE OF MEDICINE LIBRARY

fractures of this bone are extremely rare. According to Gilbert and Johnson (1966), they seem to be rare in military recruits as well, but more common than previously stated. In the present material the fractures of MT I represented 11% of all stress fractures in the metatarsals. Minor intramedullary callus can easily be overlooked.

The fractures of MT IV were of the distraction type and similar to the common march fractures of MT II and MT III. The only completely displaced fracture was found among these. Fracture of this bone is mostly associated with fractures in other metatarsals (Kroening and Shelton, 1963; Devas, 1975). However, in the present material, only one patient had simultaneous fractures of MT II and MT III in the same foot.

Fracture of the base of MT V, an avulsion caused by inversion and plantar flexion of the foot, was first described by Robert Jones in 1902. Devas (1975) suggests that the stress lesion of this bone is a comparable injury. He also mentions that the fracture can occur in the shaft of the bone, too, but only concomitantly with stress fractures in other metatarsals.

In the present material the radiographs showed fractures of the "Robert Jones type" in two patients. Both were athletes and the pain had appeared during strenuous running. The question is whether a distinction can be made between a true traumatic avulsion and a stress injury. Morris and Blickenstaff (1967) classified this lesion as a fatigue fracture resulting from muscle traction. Pure stress may not always be the sole cause. A simultaneous distortion mechanism is to be presumed.

The radiographs in the two other cases were different as were the histories. In one, a tube-like callus around the shaft was seen (Fig. 4). In the other, a cortical fissure with little periosteal callus was found in the shaft (Fig. 5). In the first case, the pain gradually increased after exercise, while in the second, the history of pain was more obscure. These cases seem to represent real stress injuries of distraction type. No stress fractures were found in other metatarsals of these patients.

The radiological images of the fractures in the cuneiform bones and in the talus were of compression type. A compression mechanism in the injuries of these spongy bones without diaphysis that make part of the foot valve seems to be apparent.

Sesamoids of the hallux are often bipartite. As radiological signs of fracture, sharp contours and diastasis of the fragments have been mentioned (Bizarro, 1921; Meschan, 1973). The X-ray of the lateral sesamoid in our case showed a characteristic avulsion with sharp borders. The history was of stress injury. The tendons of M. adductor hallucis and M. hallucis brevis partially insert in this bone. Thus, the mechanism seems to be fatigue fracture resulting from muscle traction. The previous reports in the literature concern only cases involving the medial sesamoid, (Tobold, 1903; Golding, 1960; Devas, 1975; Orava *et al.*, 1978).

Os peroneum is a sesamoid in the tendon of M. peroneus longus. The radiograph with diastasis (Fig. 7) seems to indicate an avulsion-distraction injury, but also perhaps an osteochondrotic condition (Golding, 1960). However, the history was of a stress fracture and the bone was painful.

It can be presumed that more stress injuries occur in the bones of the foot than are diagnosed. Isotope examinations of both legs in patients with stress fractures have shown that foci of increased activity appear relatively often, especially in the tarsal region, without positive radiological findings (Meurman and Elfving, 1980). Prather *et al.* (1977) reported a positive scintiscan twice in MT I without radiographic abnormality in a group of 42 patients. In the present material ten patients had more than one bone involved, two having three bones involved and two having four. Thus a careful anamnesis, meticulous clinical examination and the concomitant use of bone scanning, together with additional X-ray projections, may reveal more positive diagnoses in suspected stress injuries (Norfray *et al.*, 1980).

REFERENCES

ASAL, 1936. Überlastungsschäden am Knochensystem bei Soldaten. *Archiv für klinische Chirurgie*, *186*, 511–522.

Bernstein, A., Childers, M. A., Fox, K. W., Archer, M. C. and Stone, J. R., 1946. March fractures of the foot. Care and management of 692 patients. *American Journal of Surgery*, *71*, 355–362.

Bernstein, A. and Stone, J. R., 1944. March fracture. A report of three hundred and seven cases and a new method of treatment. *Journal of Bone and Joint Surgery*, *26*, 743–750.

Bizarro, A. H., 1921. On the traumatology of the sesamoid structures. *Annals of Surgery*, *74*, 783–791.

Childress, H. M., 1943. March fractures of the lower extremity. Report of a case of march fracture of a cuneiform bone. *War Medicine*, *4*, 152–160.

Cooper, K. H., 1968. A means of assessing maximal oxygen intake. *Journal of the American Medical Association*, *203*, 201–204.

Darby, E., 1967. Stress fractures of the os calcis. *Journal of the American Medical Association*, *200*, 1183–1184.

DeVan, W. T. and Carlton, D. C., 1954. The march fracture persists. *American Journal of Surgery*, *87*, 227–231.

Devas, M., 1975. *Stress Fractures* (Churchill Livingstone, Edinburgh/London/New York).

Geslien, G. E., Thrall, J. H., Espinosa, M. D. and Older, R. A., 1976. Early detection of stress fractures using ^{99m}Tc-polyphosphate. *Radiology*, *121*, 683–687.

Gilbert, R. S. and Johnson, H. A., 1966. Stress fractures in military recruits—a review of twelve years' experience. *Military Medicine*, *131*, 716–721.

GOLDING, C., 1960. The sesamoid of hallux. Museum pages. *Journal of Bone and Joint Surgery*, *42B*, 840–843.

JONES, R., 1902. Fracture of the fifth metatarsal bone. *Liverpool Medicochirurgical Journal*, *22*, 103–107.

KIRCHNER, A., 1905. Die Aetiologie der indirecten Metatarsalfracturen. *Archiv für klinische Chirurgie*, *77*, 241–267.

KROENING, P. M. and SHELTON, M. L., 1963. Stress fractures. *American Journal of Roentgenology*, *89*, 1281–1286.

MASERITZ, I. H., 1936. March foot associated with undescribed changes of the internal cuneiform and metatarsal bones. *Archives of Surgery*, *32*, 49–64.

MAURER, R., 1970. Die Marschfrakturen der unteren Extremität und des Beckens. Eine Untersuchung anhand von 160 Fällen der Schweizer Armee aus den Jahren 1965 und 1966. *Schweizerische Zeitschrift für Militärmedizin*, *47*, 60–84.

MESCHAN, I., 1973. *Analysis of Roentgen Signs in General Radiology* Vol 1 (Saunders, Philadelphia).

MEURMAN, K. O. A., 1980. Stressläsionen des Talus. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklear medizin*, *132*, 469–471.

MEURMAN, K. O. A. and ELFVING, S., 1980a. Stress fracture of the cuneiform bones. *British Journal of Radiology*, *53*, 157–160.

1980b. Stress fracture in soldiers: a multifocal bone disorder. A comparative radiological and scintigraphic study. *Radiology*, *134*, 483–487.

MORRIS, J. M. and BLICKENSTAFF, L. D., 1967. *Fatigue Fractures. A Clinical Study.* (Charles C. Thomas, Springfield, Illinois, USA).

NION, 1903. Mitteilungen aus der Röntgenabteilung. c.Zur Statistik der Mittelfussknochenbruche. *Deutsche Militärärztliche Zeitschrift*, *32*, 200–201.

NORFRAY, J. F., SCHLACHTER, L., KERNAHAN, W. T. Jr., ARENSON, D. J., SMITH, S. D., ROTH, I. E. and SCHLEFMAN, B. S., 1980. Early confirmation of stress fractures in joggers. *Journal of the American Medical Association*, *243*, 1647–1649.

ORAVA, S., PURANEN, J. and ALA-KETOLA, L., 1978. Stress fractures caused by physical exercise. *Acta Orthopaedica Scandinavica*, *49*, 19–27.

PRATHER, J. L., NUSYNOWITZ, M. L., SNOWDY, H. A., HUGHES, A. D., MCCARTNEY, W. H. and BAGG, J. R., 1977. Scintigraphic findings in stress fractures. *Journal of Bone and Joint Surgery*, *59A*, 869–874.

RÜCKERT, K. F. and BRINKMANN, E. R., 1975. Ermüdungsbrüche der Fersenbeine bei Soldaten der Bundeswehr. *Münchener Medizinische Wochenschrift*, *117*, 681–684.

SAVOCA, C. J., 1971. Stress fractures. *Radiology*, *100*, 519–524.

TOBOLD, 1903. Mitteilungen von der Röntgenstation. Zur Kasuistik der Mittelfussknochenbruche. *Deutsche Militärärztliche Zeitschrift*, *32*, 573–585.

WILSON, E. S. and KATZ, F. N., 1969. Stress fractures. An analysis of 250 consecutive cases. *Radiology*, *92*, 481–486.

Book reviews

An Atlas of Radiologic Anatomy. By Lothar Wicke. pp. 234, illus., 1978. (Urban and Schwarzenberg, Baltimore/Munich), £8·75.

ISBN 0–8067–2111–1 (Baltimore)
3–541–72111–1 (München)

This atlas, printed on glossy paper, is composed of 117 beautifully reproduced high quality radiographs with accompanying line drawings. The line drawings are particularly well done, and I am unaware of any book that gives a more lucid and accurate correlation between radiographic appearances and anatomical structures.

The atlas covers both plain films and contrast examinations in a systematic fashion and, where appropriate, an indication of the radiographic positioning is also given.

I could find only one serious error in the book and that is unfortunately on the first page of the text (p.9), where an explanation of radiographic projections and patient orientation is given. The figures in the text in this section do not correspond to the figures in the accompanying diagram. Another criticism of the book is that many readers will find the use of the Nomina Anatomica rather cumbersome (*e.g.* Bulbus venae jugularis internae dexter et sinister=jugular bulbs). The nomenclature may prove confusing to students using the book in conjunction with standard texts on procedure and positioning in which conventional terminology is used. These drawbacks, however, are minor ones and do not really detract from the excellence of the book as an atlas of radiology.

In summary, this book provides a comprehensive review of radiological anatomy which will not only prove useful to the part I F.R.C.R. student and the radiographer in training, but will also be valuable for reference and revision. It is an indispensable addition to the library shelves of every teaching department.

D. J. ALLISON.

Disorders of the Cervical Spine. By Eurig Jeffreys. pp. ix+147, illus., 1980 (Butterworth, London) £25·00.

ISBN 0–407–00158–1

This monograph, written by an orthopaedic surgeon, surveys the gamut of disease that may afflict the cervical spine. There is a contribution on fractures and dislocation by another famous Oswestrian, Mr. Terence McSweeney.

The book is divided into ten chapters, one each dealing with applied anatomy, radiology, and surgical procedures. The remaining seven deal with disease grouped on a pathological basis. It is liberally sprinkled with radiographs and with anatomical line drawings. Each chapter concludes with a full bibliography and there is an adequate index.

Mr. Jeffreys writes in an almost conversational style, with numerous quotable quotes and witty asides. On occasion, perhaps, these prove a little excessive, although I admit I am now much wiser about the afflictions of King Richard III.

Radiologists will be disappointed by the poor quality of many of the illustrations. In many cases the lesion is not readily appreciated, or dare it be said, contentious in its interpretations. Anatomists may be puzzled by a diagrammatic representation of the anterior spinal artery with a calibre at least as great as that of the vertebral (Figure 1.17).

This very readable and enjoyable book is written primarily for orthopaedic surgeons. However, as the author himself points out, there are many other specialists who share a common interest in this area of the anatomy, radiologists not the least. This book will be an amusing and informative acquisition to all who have a particular interest in musculo-skeletal radiology, though I doubt whether the average trainee will greatly benefit from studying it assiduously.

I. WATT.

1981, *British Journal of Radiology*, *54*, 8–11

Bilateral renal cell carcinoma—unusual occurrence in three members of one family

By E. R. Reddy, M.D., D.M.R.D., F.R.C.R.*

Department of Radiology, Newcastle General Hospital and Freeman Hospital, Newcastle upon Tyne

(*Received March 1980 and in revised form July 1980*)

ABSTRACT

Bilateral renal cell carcinoma occurred in a father and his two sons. Other reported instances of familial renal cell carcinoma are reviewed and the possibility that renal cell carcinoma might have a familial tendency is discussed. Radiological investigation and screening of suspected families is stressed.

Renal cell carcinoma is a relatively common malignant neoplasm of the kidney. Though synchronous or metachronous bilateral renal cell carcinoma can occur, predominantly it is a unilateral neoplasm. Unlike tumours of the breast, colon or endometrium which commonly show a familial pattern (Lynch, 1967), renal cell carcinoma occurring in families is unusual. Because of the rarity of the condition, I wish to report bilateral renal cell carcinoma occurring in a father and his two sons, proved by either biopsy or autopsy.

CASE REPORTS

Case 1

The younger of two brothers presented at the age of 37 years with a history of left loin pain of one week's duration. There was no history of haematuria or any urinary symptoms. On physical examination the left kidney was palpable and mobile; Hb 14.8 g%, blood pressure 130/80 mmHg, ESR 21 mm/hr, blood group A positive. Examination of the urine did not show any abnormality. An excretory urogram (Fig. 1A) was done, followed by bilateral selective renal arteriograms. The right side was interpreted as normal. The selective left renal arteriogram is shown in Fig. 1B. A chest radiograph and ^{99}Tc^{m} bone scan showed no evidence of metastases.

The patient had a left nephrectomy. At operation a number of small cysts of the pancreas were also noted. He was symptom-free for five years and later presented with a palpable mass in the right lumbar region, joint pains and urethritis. At this time his ESR was 120 mm/hr, and no other significant abnormality was detected in the laboratory investigations. A chest radiograph and ^{99}Tc^{m} bone scan showed no evidence of metastases. An excretory urogram showed a rather bulky lower pole of the right kidney without calyceal distortion. A selective renal arteriogram (Fig. 1C) was abnormal and interpreted as a renal carcinoma. The patient had a right lower pole nephrectomy. He has remained symptom-free for one year.

On macroscopic examination of the left kidney, there was an oval shaped yellow-red tumour at the lower pole 5 cm in diameter. One of the cysts, 2 cm in diameter, contained yellow tissue which appeared to be a tumour. This was situated on the posterior wall of the kidney. Histological examination revealed a clear cell carcinoma in both the regions, and no connection was demonstrated between the two neoplasms. Histological examination of the lower pole of the right kidney also showed the presence of a clear cell renal carcinoma.

Case 2

The elder of two brothers, presented at the age of 39 years with a history of pain in both loins, particularly on the right side. On physical examination the right kidney was palpable and felt enlarged; blood pressure 140/90 mmHg, Hb 11.9 g%, blood group A positive. An excretory urogram (Fig. 2A) and bilateral selective renal arteriograms were done. Changes on the right side were interpreted as consistent with a renal cell carcinoma. A chest radiograph and ^{99}Tc^{m} bone scan showed no evidence of metastases. The patient had a right nephrectomy. Histopathological examination showed clear cell carcinoma of the kidney. On the left side the selective renal arteriogram (Fig. 2B) was interpreted as a benign adenoma or a renal cell carcinoma. Consequently the patient also had a left lower pole nephrectomy. Histopathological examination confirmed the presence of a clear cell carcinoma. There were also small cysts in the upper pole and lower pole. Later the patient moved to a different part of the country and died one year after the operation. No details are available as to the cause of the death, and no post-mortem report is available.

Case 3

The father of the above two patients died at the age of 63 with a history of myocardial infarction. However, at post-mortem, bilateral renal cell carcinomata were found. No other relevant details of the post-mortem report are available.

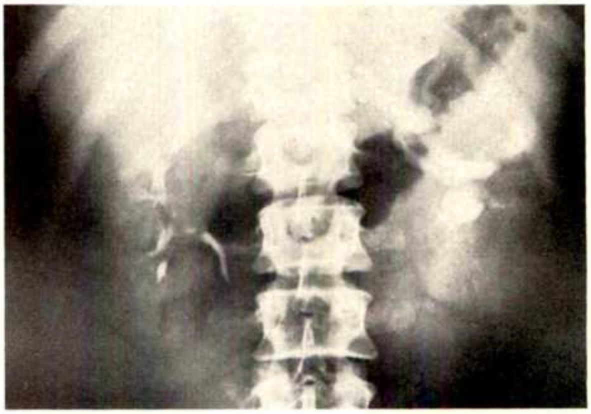


FIG. 1A.

Excretory urogram of Case 1, shows distortion of the calyces in the upper and lower poles of the left kidney suggesting space occupying lesions.

---

*Present address: Radiologist, Curtis Memorial Hospital, St. Anthony, Newfoundland, Canada, AOK 4SO.

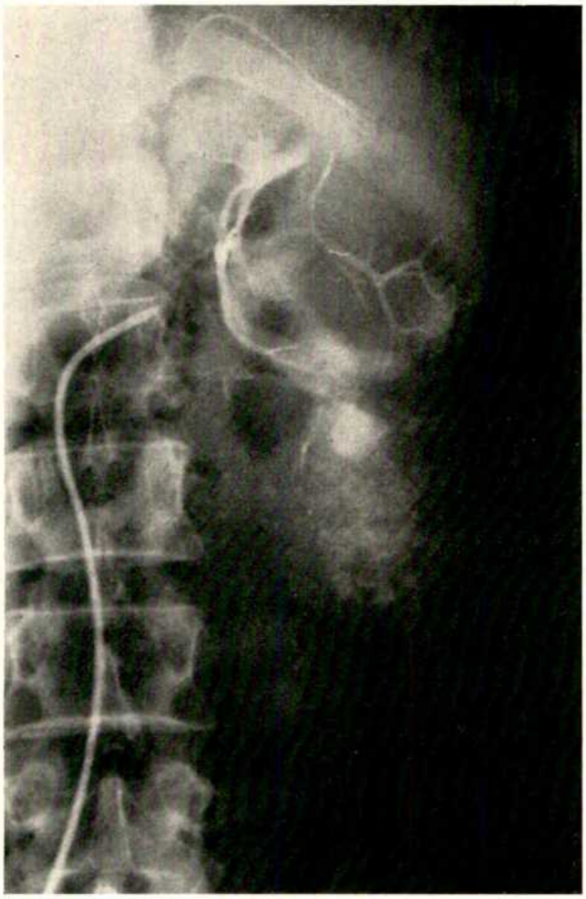


FIG. 1B.

Selective left renal arteriogram of Case 1 shows abnormal vessels and vascular blush in the lower pole and also an area of abnormal vascularity in the upper pole on the lateral aspect.

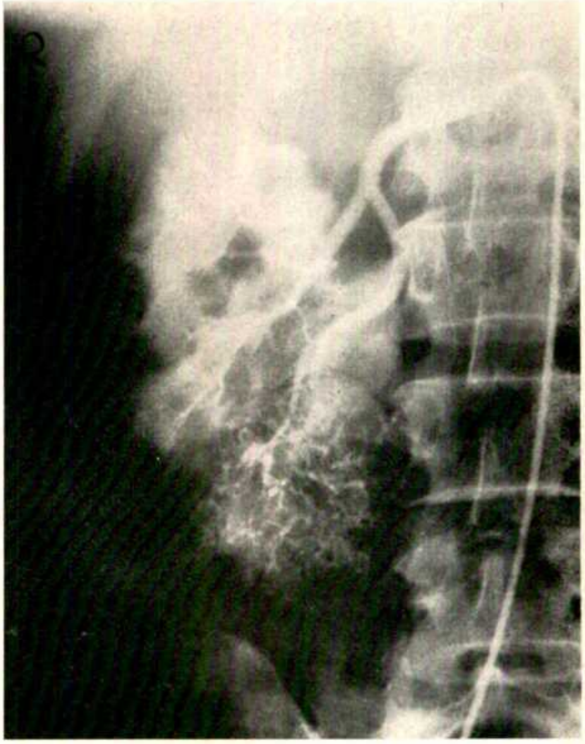


FIG. 1C.

Selective right lower pole renal arteriogram (there were two renal arteries on the right side) of Case 1, five years after the initial radiographs and left nephrectomy, shows an area of abnormal vascularity in the lower pole.

DISCUSSION

A literature review is presented in Table I. Familial incidence is rare in renal cell carcinoma, although there is high frequency in patients with Lindau-Von Hippel disease (Kaplan *et al.*, 1961). Occurrence of bilateral renal cell carcinoma (Small *et al.*, 1968; Hyman *et al.*, 1973), and the development of renal cell carcinoma in association with polycystic disease of the kidney (McFarland *et al.*, 1972), is rare but well documented. The patient in case 1 had two cysts in the left kidney and a few cysts were also noted in his pancreas at the time of nephrectomy. The patient in case 2 was also found to have small cysts in the left kidney at the time of surgery. Otherwise, no clinical or radiological evidence of Lindau-Von Hippel disease was seen in our patients. The present cases are also interesting in that in two siblings the diagnosis was suggested preoperatively on the basis of radiological examination. There was no radiological evidence of metastases. All tumours were macroscopically well demarcated, and microscopic examination revealed a consistent pattern of clear cell carcinoma. Similar consistent patterns of histological appearances of the tumours were also reported by Franksson *et al.* (1972) and Guirguis (1973) in their series. It is interesting to note that both the siblings in the series were blood group A positive, in which higher inheritance susceptibility to renal cell carcinoma has been reported by Desai and Brown (1976).

The occurrence of bilateral renal cell carcinoma is an ominous sign, usually indicating a poor prognosis. Various criteria have been suggested to establish the diagnosis of bilateral tumours whether they are primary or metastatic (Small *et al.*, 1968; Hyman *et al.*, 1973; Stroup *et al.*, 1974). However it appears that no characteristics exclusively distinguish bilateral primary renal cell carcinoma from unilateral tumour metastasising to the opposite side. In the

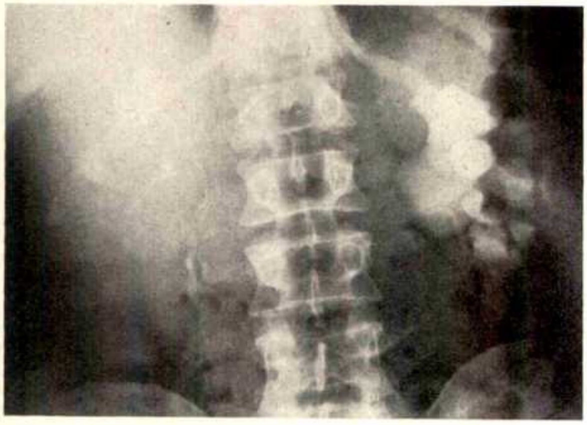


FIG. 2A.

Excretory urogram of Case 2, shows enlarged right kidney with calyceal distortion suggesting a space occupying lesion and dilatation of the pelvicalyceal system on the left side which was interpreted as due to congenital pelvi-ureteric obstruction.

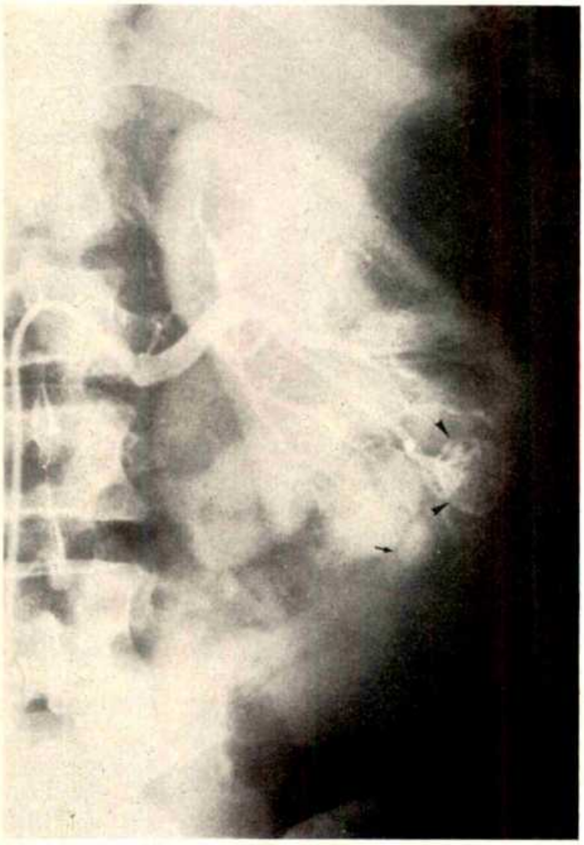


FIG. 2B.

Selective left renal arteriogram of Case 2, shows a circular area of abnormal vascularity within well defined margins (arrow heads) in the lower pole. The oval opacity in the lower pole (single arrow) was a calculus, noted also on the preliminary film.

TABLE I

SUMMARY OF PREVIOUSLY REPORTED CASES OF FAMILIAL RENAL CELL CARCINOMA

Author	Year	Number	Comments
Clemmesen	1942	2	A family of 15 siblings of whom 2 had renal cell carcinoma and 6 had polycystic kidneys.
Rusche	1953	2	Brothers. Primary lesion was silent and the diagnosis was made after biopsy of the metastatic lesion.
Krumback and Ansell	1959	1	Bilateral multiple renal cell carcinoma Father had died of renal cell carcinoma.
Brinton	1960	3	Father also said to have died of kidney tumour.
Griffin *et al.*	1967	2	Mother and son
Klinger	1968	2	Brother and sister
Pearson	1969	3	All 3 had hypertension.
Steinberg *et al.*	1972	2	Mother and daughter
Franksson *et al.*	1972	5	All siblings. 4 had multiple bilateral tumours and other had a solitary tumour in 1 kidney.
Guirguis	1973	4	Mother and 3 sons.
Braun *et al.*	1975	8	In 4 separate families and reported high frequency of HLA–W17 both in the patients and in apparently unaffected family members.
Lyons *et al.*	1977	2	Brothers.
Pilepich *et al.*	1978	2	Brothers. Reported the presence of a common haplotype A2B W21.
Cohen *et al.*	1979	10	In 1 family from 3 generations and also showed chromosomal translocation.

absence of demonstrable metastases elsewhere in the body, similar histological type of cells, simultaneous occurrence and multiplicity of the lesions probably suggest that the neoplasms are primary.

The occurrence of renal cell carcinoma in two brothers and in their father may be coincidence. If a genetic factor is present the question of screening other members of the family arises (not done here). Recently Cohen *et al.* (1979) reported renal cell carcinoma in ten members of a family from three consecutive generations, and showed balanced reciprocal chromosomal translocation between chromosomes three and eight. They provided the karyotypic evidence that an inherited genetic abnormality predisposes to hereditary renal cell carcinoma. The cancers tended to develop at earlier ages and to occur in both the kidneys at multiple sites by comparison with non-familial renal cell carcinoma. The familial occurrence of the renal cell carcinoma can be tackled by means of genetic counselling and amniocentesis to identify carriers of the chromosomal translocation *in utero* (Cohen *et al.*, 1979; Golbus *et al.*, 1979). Cohen *et al.* (1979) suggested that mortality from metastatic renal cell carcinoma justified screening. In their series three members without symptoms were found to have bilateral renal cell carcinoma on the basis of intravenous pyelograms performed during screening studies of 20 adult family members.

The evidence suggests that radiological investigations are mandatory in every instance of suspected familial renal cell carcinoma, not only at the time of initial examination but also at follow-up.

ACKNOWLEDGMENTS

I wish to thank Dr. W. Simpson and Dr. J. R. Young for permission to publish these cases and for their advice, Miss Audrey Kellet for preparing the photographs, Mrs. Agnes Budgell and Miss Jean Noel for typing the manuscript.

REFERENCES

BRAUN, W. E., STRIMLAN, C. V., NEGRON, A. G., STRAFFON, R. A., ZACHARY, A. A., BARTEE, S. L. and GRECEK, D. R., 1975. The association of W17 with familial renal cell carcinoma. *Tissue Antigens*, *6*, 101–104.

BRINTON, L. F., 1960. Hypernephroma—Familial occurrence in one family. *Journal of the American Medical Association*, *173*, 889–890.

CLEMMESEN, J., 1942. Combined familial occurrence of malignant hypernephroma and renal cysts. *Nordisk Medicin*, *14*, 1472–1476.

COHEN, A. J., LI, F. B., BERG, S., MARCHETTO, D. J., TSAI, S., JACOBS, S. C. and BROWN, R. S., 1979. Hereditary renal-cell carcinoma associated with a chromosomal translocation. *New England Journal of Medicine*, *301*, 592–595.

DESAI, M. and BROWN, H. E., 1976. ABO blood group in relation to hypernephroma, *Urology*, *3*, 596–597.

FRANKSSON, C., C., BERGSTAND, A., LJUNGRAH, I., MANUSSON, G. and NORDENSTRAM, H., 1972. Renal carcinoma (hypernephroma) occurring in five siblings. *Journal of Urology*, *100*, 58–61.

GRIFFIN, J. P., HUGHES, G. N. and PEELING, W. B., 1967. A survey of the familial incidence of adenocarcinoma of the kidney. *British Journal of Urology*, *39*, 63–66.

GOLBUS, M. S., LOUGHMAN, W. D., EPSTEIN, C. J., HALBASCH, G., STEPHENS, J. D. and HALL, B. D., 1979. Prenatal genetic diagnosis in 3000 amniocenteses. *New England Journal of Medicine*, *300*, 157–163.

GUIRGUIS, A. B., 1973. Renal cell carcinoma—unusual occurrence in four members of one family. *Urology*, *2*, 283–285.

HYMAN, R. A., VOGES, V. and FINBY, N., 1973. Bilateral hypernephroma. *American Journal of Roentgenology*, *117*, 104–107.

KAPLAN, C., SAYRE, G. P. and GREENE, L. P., 1961. Bilateral nephrogenic carcinoma in Lindau-Von-Hippel disease. *Journal of Urology*, *86*, 36–42.

KLINGER, M. E., 1968. Renal cell carcinoma in siblings. A case report. *Journal of the American Geriatric Society*, *16*, 1047–1052.

KRUMBACH, R. W. and ANSELL, J. S., 1959. Partial removal of the right kidney and radical removal of the left kidney in a patient with bilateral hypernephroma. *Surgery*, *45*, 585–588.

LYNCH, H. T., 1967. Hereditary and the more common malignancies of man. Carcinoma of the breast, stomach, colon, lung, prostate and endometrium. In *Hereditory Factors in Carcinoma* (Springer-Verlag, New York), pp. 35–53.

LYONS, A. R., 1977. Hypernephroma in two brothers. *British Medical Journal*, *1*, 816–817.

MCFARLAND, W. L., WALLACE, S. and JOHNSON, D. E., 1972. Renal carcinoma and polycystic disease. *Journal of Urology*, *107*, 530–532.

PEARSON, H. H., 1969. Familial renal tumours. *Australian and New Zealand Journal of Surgery*, *38*, 333–338.

PILEPICH, M. N., BERKMAN, E. M. and GOODCHILD, N. T., 1978. HLA typing in familial renal carcinoma. *Tissue Antigens*, *11*, 487–488.

RUSCHE, C., 1953. Silent adenocarcinoma of the kidney with solitary metastasis occurring in brothers. *Journal of Urology*, *70*, 146–151.

SMALL, M. P., ANDERSON, E. E. and ATWILL, W. H., 1968. Simultaneous bilateral renal cell carcinoma. Case report and review of the literature. *Journal of Urology*, *100*, 8–14.

STEINBERGH, S. M., BRODOVSKY, H. S. and GOEPP, C. E., 1972. Renal carcinoma in mother and daughter. *Cancer*, *29*, 222–225.

STROUP. R. F., SHEARER, J. K., TRAWRING, A. R. and LYLTON, B., 1974. Bilateral adenocarcinoma of the kidney, treated by nephrectomy. A case report and review of the literature. *Journal of Urology*, *111*, 272–276.

1981, *British Journal of Radiology*, 54, 12–14

Aging and simple cysts of the kidney

By S. P. Laucks, Jr., M.D., Ph.D. and M. S. F. McLachlan, M.D.

Department of Radiology, The University of Rochester, Strong Memorial Hospital, Rochester, NY 14642, USA

(*Received July 1980*)

ABSTRACT

Abdominal CT scans of 103 patients without evidence of renal disease were examined. Unsuspected simple renal cysts were demonstrated in 25 (24%). No cysts were demonstrated in patients less than 40 years old. Thereafter the number of cysts and the number of patients with cysts tended to increase with age. Cyst dimensions also increased. These observations suggest that the development of simple cysts of the kidney is related to aging.

Evidence from pathologists (Councilman, 1919; Kissane, 1974), surgeons (Braasch and Hendrick, 1944) and from computerized tomography (CT) (Hattery *et al.*, 1977) suggests that simple cysts of the kidney are common in later life. None of these studies assessed the prevalence of cysts or the extent to which their development is related to aging, though Kissane (1974), apparently basing his conclusions on surgical and necropsy evidence, considered that "gross cysts" occurred in at least 50% of people over 50 years old.

We have examined the frequency with which unsuspected simple cysts are demonstrated on CT scans of the abdomen, performed for reasons other than investigation of renal disease. To examine how closely the development of cysts is associated with aging, we have related the number of cysts and their dimensions to the age of the patient.

MATERIAL AND METHODS

All CT scans of the abdomen obtained at Strong Memorial Hospital between September, 1977 and July, 1979 were reviewed. They were performed on a General Electric 7800 (before January, 1979) or 8800 (during and after January, 1979) whole body scanner and 103 patients were included in the study. They had been examined for reasons unrelated to the upper urinary tract, usually for suspected or known intra-abdominal malignancy or disease of the pancreas or biliary system. Apart from the existence of simple cysts (defined below), kidneys were normal on CT scan. Fifty-four were males aged two days to 82 years (mean 58 years); 49 were female, aged nine months to 83 years (mean 56 years). The whole of both kidneys was included before and after intravenous injection of 50 ml Renografin 60 (sodium and meglumine diatrizoate; Squibb). Scan times were 9.6 seconds. Slice thickness was 10 mm. Scans were performed at 10 mm intervals in 81 patients and 20 mm intervals in 22. Simple cysts were defined as small thin-walled renal masses of uniform density, with an attenuation coefficient approximating to water value, which were not enhanced by intravenous contrast medium (Hattery *et al.*, 1977). The greatest transverse diameter of each cyst was measured: filmed images were projected to approximately twice life size and actual dimensions calculated by comparison with a reference grid.

RESULTS

Simple cysts were observed in 25 of the 103 patients (24%). Figure 1 shows the proportion of patients with cysts by decade. No cysts were observed in patients under 40 years old. Thereafter, cysts became more common, the total number of cysts and the number of patients affected being significantly greater after the sixth decade ($p < 0.01$–0.001; Fig. 2). The number of cysts per patient ranged from one to six. Cyst diameter was 0.55 to 7.25 cm (mean 2.33 cm), dimensions tending to increase with age (Fig. 3). No differences were observed between males and females or right and left kidneys. The frequency with which cysts were

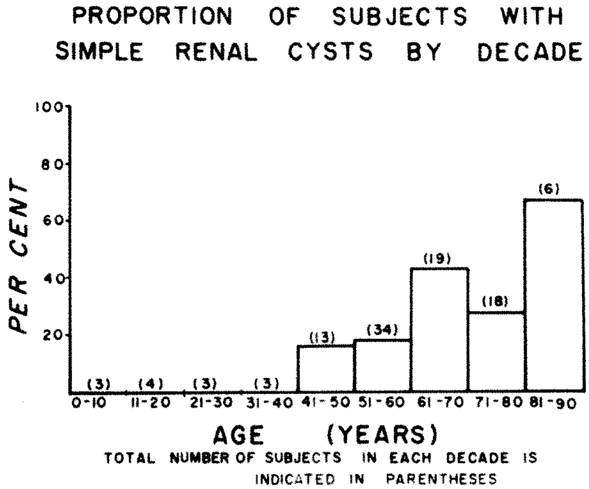


FIG. 1.

Simple renal cysts occurred in about 20% or more of subjects over 40 years old. After that the proportion tended to increase with age. No cysts were observed before the age of 40.

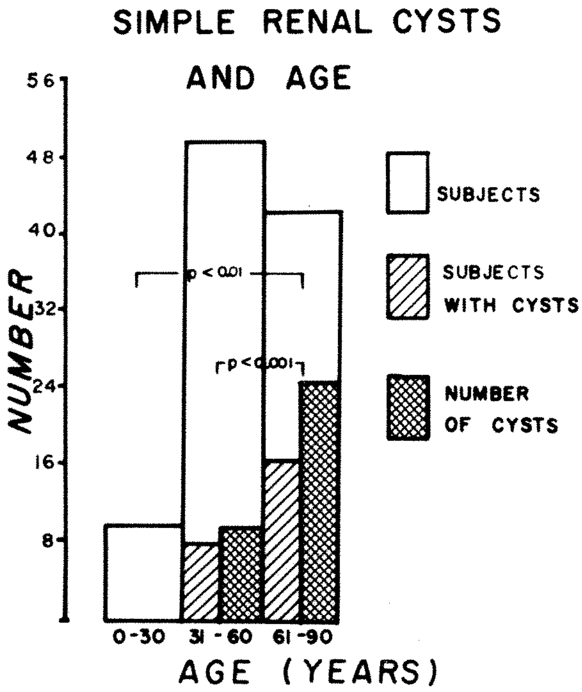


FIG. 2.

The number of cysts per subject also increased with age. Significance levels above the bars refer to the number of subjects and the number of cysts.

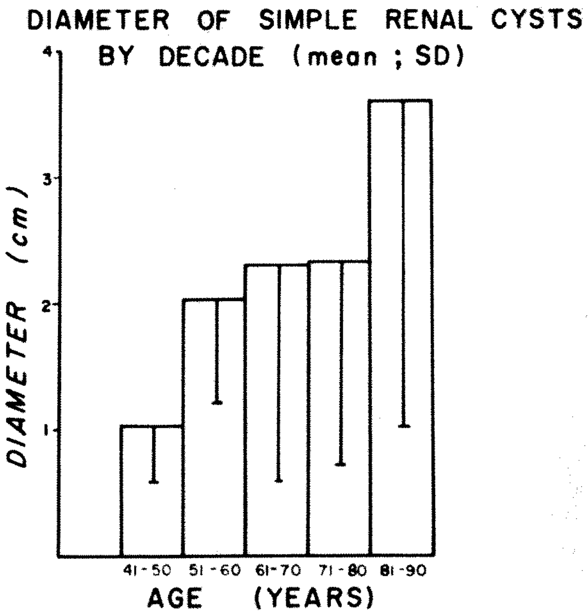


FIG. 3.

Cyst diameter tended to increase with age. It ranged from 0.55 to 7.25 cm (mean 2.33 cm).

observed was not related to the interval between slices.

DISCUSSION

For many years, pathologists (Councilman, 1919; Kissane, 1974) and surgeons (Braasch and Hendrick, 1944) have recognized that simple cysts of the kidney are common after middle age. These studies are restricted in their scope. By their nature, they cannot define the prevalence of symptomless cysts in apparently healthy individuals. A relationship between age and the development of cysts, though implied, is not established. More recently, computerized tomography has provided evidence *in vivo* that cysts are "frequent incidental findings" in the elderly (Hattery *et al.*, 1977). Again these observations stop short of defining the prevalence of simple cysts or their relationship with age. Our experience confirms and extends these observations.

Simple cysts are very common. After the age of 40, they occurred in at least 20% of patients with no other evidence of renal abnormality; after the sixth decade the proportion approached one-third. Moreover, as age advanced, it became more likely that a kidney would contain more than one cyst. The dimensions of cysts also increased, their mean diameter, 1 cm in the fifth decade, doubled thereafter. We have occasionally documented this enlargement by urography (Fig. 4).

These observations strengthen the view (Kissane, 1974) that simple cysts are acquired. Hepler (1930), who also held this opinion, provided experimental support when he produced cysts in the rabbit by simultaneously infarcting kidney segments and obstructing tubules. He pointed out that the likelihood of infarction and tubular obstruction increases with age; renal arterial and arteriolar sclerosis become more marked (Bell, 1950) and tubular obstruction may follow an age-related increase in renal medullary interstitial fibrosis (Helpap, 1933; Keresztury and Megyeri, 1962). Others (Baert and Steg, 1977) have suggested that cysts result from enlargement of diverticula of the distal convoluted and collecting tubules. This explanation too implies a relationship with aging; diverticula increase in number in the senescent kidney, probably as a result of weakening of tubular basement membrane (Darmady *et al.*, 1973).

The frequency with which cysts occur raises issues about the management of patients in whom a renal mass is demonstrated as an incidental finding. Kissane (1974) argued from pathological evidence that cysts occur in at least 50% of persons over 50 years of age, twice as commonly as our observations suggest. It is unlikely that this large number will be discovered in life. Some will be overlooked at urography, even with tomography and high doses of contrast agent (Hattery *et al.*, 1976). CT scans may also fail to reveal them because of partial volume effects and changes in position due to respiration (Hattery *et al.*, 1977). Though we saw cysts equally frequently on scans performed at 10 and 20 mm intervals, small cysts may not have been demonstrated. If simple cysts are fortuitously revealed on CT scans, should they be investigated further? Like McClennan *et al.* (1979), we can no longer justify diagnostic aspiration of lesions which possess the characteristics of simple cysts on CT scanning (Hattery *et al.*, 1977). We emphasize, however, that this change in our policy has not affected our management of masses which do not conform to these criteria.

ACKNOWLEDGMENT

We thank Dr. Derek Hamlin for his help.

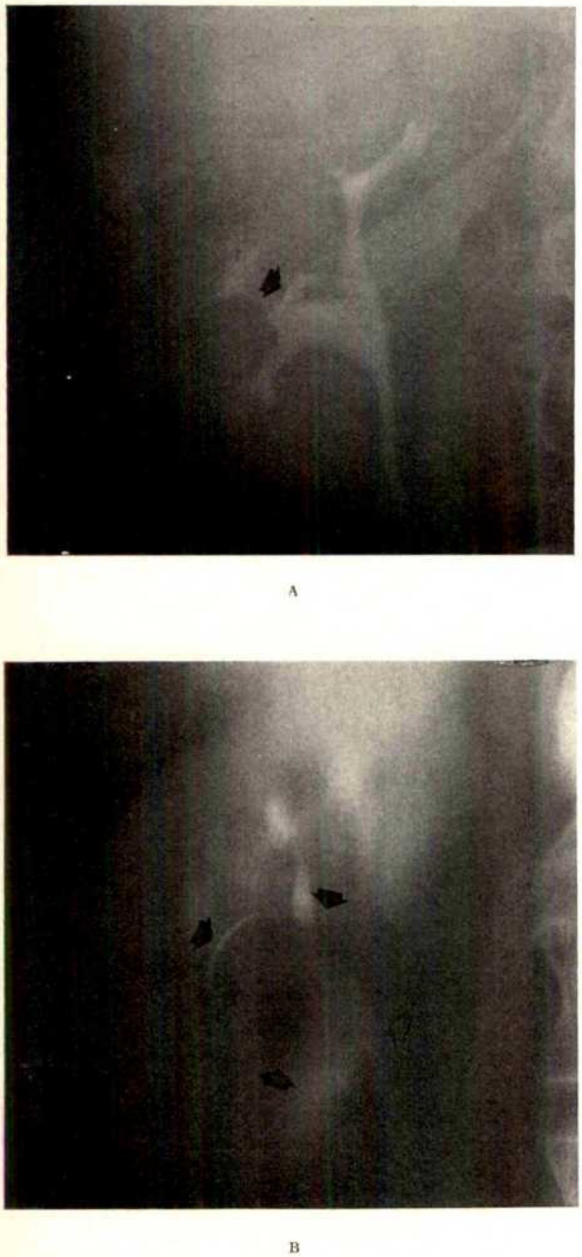


FIG. 4.

Intravenous urography shows enlargement of a simple cyst of the right kidney, first demonstrated (arrowed in A) when this man was 69 years old. Twelve years later (B, arrows), the cyst has nearly doubled in size. (Not from series.)

REFERENCES

BAERT, L. and STEG, A., 1977. Is the diverticulum of the distal and collecting tubules a preliminary stage of the simple cyst in the adult? *Journal of Urology*, *118*, 707–710.

BELL, E. T., 1950. *Renal Disease* 2nd edition, (Lea & Febiger, Philadelphia) pp. 331–346.

BRAASCH, W. F. and HENDRICK, J. A., 1944. Renal cysts, simple and otherwise. *Journal of Urology*, *51*, 1–10.

COUNCILMAN, W. T., 1919. The conditions presented in the heart and kidneys of old people. In *Contributions to Medical and Biological Research, dedicated to Sir William Osler*, (Paul B. Hoeber, New York) pp. 918–928.

DARMADY, E. M., OFFER, J. and WOODHOUSE, M. A., 1973. The parameters of the aging kidney. *Journal of Pathology*, *109*, 195–207.

HATTERY, R. R., WILLIAMSON, B. and HARTMAN, G. W., 1976. Urinary tract tomography. *Radiological Clinics of North America*, *14*, 23–49.

HATTERY, R. R., WILLIAMSON, B., STEPHENS, D. H., SHEEDY, P. F. and HARTMAN, G. W., 1977. Computed tomography of renal abnormalities. *Radiological Clinics of North America*, *15*, 401–418.

HELPAP, K., 1933. Über aufsteigende Schrumpfniere durch Sklerose des Nierenmarks. *Virchows Archiv; Abteilung A: Pathologische Anatomie*, *288*, 383–392.

HEPLER, A. B., 1930. Solitary cysts of the kidney. *Surgery, Gynecology and Obstetrics*, *50*, 668–687.

KERESZTURY, S. and MEGYERI, L., 1962. Histology of renal pyramids with special regard to changes due to aging. *Acta Morphologica Academiae Scientiarum Hungaricae*, *11*, 205–215.

KISSANE, J. M., 1974. Congenital malformations. In *Pathology of the Kidney* Ed. R. H. Heptinstall (Little & Brown Co, Boston), pp. 69–119.

MCCLENNAN, B. L., STANLEY, R. J., MELSON, G. L., LEVITT, R. G. and SAGEL, S. S., 1979. CT of the renal cyst: is cyst aspiration necessary? *American Journal of Roentgenology*, *133*, 671–675.

1981, *British Journal of Radiology*, *54*, 15–17

Lymphograms in prostatic carcinoma: false-positive and false-negative assessments in radiology

By T. Sherwood, F.R.C.R.*, and E. P. N. O'Donoghue, F.R.C.S.

Institute of Urology and St. Peter's Hospitals, London

(*Received June 1980*)

ABSTRACT

Forty patients with prostatic carcinoma underwent lymphography and pelvic lymphadenectomy. Node-by-node comparisons between radiology and histology findings yielded high false-negative rates for the lymphogram as a staging tool. False-positive and false-negative rates depend on the viewpoint taken: we argue that these rates should be expressed in terms of the disease, not the *in vivo* test. Lymphography has serious defects as a staging manoeuvre, but pelvic lymphadenectomy carries greater morbidity and mortality in its train.

False-positive and false-negative rates are frequently quoted in papers on the value of diagnostic tests. They are highly ambiguous terms (*Lancet*, 1979). We report a node-by-node comparison between lymphograms and pelvic lymphadenectomy in patients with prostatic carcinoma, highlighting this problem.

PATIENTS AND METHODS

Patients with histologically confirmed carcinoma of the prostate were referred to our centre from a variety of other hospitals. To stage the disease we first performed a radionuclide bone scan (O'Donoghue *et al.*, 1978). If bone deposits are shown by this technique coupled with radiographic skeletal surveys, the patient clearly has widely disseminated disease. More detailed staging by invasive procedures then appears meddlesome and unnecessary.

If bone deposits were not detected, we assessed whether our patients were fit for lymph node staging. Age, frailty or respiratory impairment were grounds for not pressing on with such studies. In the absence of contraindications, patients were asked to have a lymphogram, followed at least two weeks later by a limited laparotomy for pelvic lymph node dissection. Details of protocol, lymphogram assessment and surgery have already been reported (O'Donoghue *et al.*, 1976).

In a group of 90 untreated patients with prostatic carcinoma we found 56 with no evidence of bone deposits (O'Donoghue *et al.*, 1978). This paper reports on the lymph node studies offered to 40 of these patients.

We carried out a node-by-node comparison between lymphogram and the histology report of removed nodes. Identification of nodes on pre- and post-operative films was aided by marking the bed of each dissected node with a metal clip at surgery. The lymphograms were first read "blind" by both of us (radiologist and surgeon). In view of our results we later asked two radiologists with special experience in lymphography to review all lymphograms, providing further views for assessment (Table III).

RESULTS

Table I shows the results of comparing histological and radiological findings node-by-node. This table is set out as such comparisons are commonly made: from the point of view of the clinician or radiologist judging an *in vivo* test against histological criteria. There is clearly a considerable error rate, with an accuracy of only 60%. However, most positive lymphogram results are corroborated by histology, with an apparent false-positive rate of 33%. Most negative lymphogram results are also confirmed, with an apparent false-negative rate of 43%.

The same data is set out again in Table II, but now from the viewpoint of the histopathologist as arbiter. The answers are different.

Table III shows the 23 patients in whom the two additional specialist radiologists agreed with the original lymphogram assessment. It is set out in the same way as Table II, and shows that there is a small gain in this combined approach.

TABLE I

NODE-BY-NODE COMPARISON: THE TEST

		Lymphogram findings	
	40 patients	positive 12	negative 28
Lymphadenectomy findings	negative	4	16
	positive	8	12

Lymphogram accuracy $\frac{24}{40}=60\%$

False-positive results $\frac{4}{12}=33\%$

False-negative results $\frac{12}{28}=43\%$

---

*Present address: Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

TABLE II

Node-by-node comparison: the disease

	40 patients	Lymphadenectomy findings	
		positive 20	negative 20
Lymphogram findings	positive	8	4
	negative	12	16

Lymphogram accuracy $\frac{24}{40}=60\%$

True-positive rate $\frac{8}{20}=40\%$ (sensitivity)

False-negative rate $\frac{12}{20}=60\%$

True negative rate $\frac{16}{20}=80\%$ (specificity)

False-positive rate $\frac{4}{20}=20\%$

TABLE III

Node-by-node comparison: unanimous judgements by four observers

	23 patients	Lymphadenectomy findings	
		positive 10	negative 13
Lymphogram findings	positive	5	2
	negative	5	11

Lymphogram accuracy $\frac{16}{23}=70\%$

True-positive rate $\frac{5}{10}=50\%$

False-negative rate $\frac{5}{10}=50\%$

True-negative rate $\frac{11}{13}=85\%$

False-positive rate $\frac{2}{13}=15\%$

Discussion

A question commonly asked by clinicians or radiologists about the accuracy of *in vivo* tests runs "if we do 100 tests, how often will we be wrong?". The traditional answers, in terms of false-positive and false-negative rates, express the proportion of patients with a positive or negative test result which does not match the presence or absence of disease. Current teaching (McNeil *et al.*, 1975) recognizes that it is more useful to put different questions. These run "if a patient has the disease, what is the likelihood that the test will be positive?". Or: "if the patient does not have the disease, what are the chances that the test will correctly identify him by giving a negative result?"

It will be noted that the new questions involve simply a change in perspective, illustrated by the fact that the same data has been turned through a right angle between Tables I and II. From the new stance overall accuracy is of course identical, but false-positive and false-negative rates are different. Table II indicates that in our practice the lymphogram will only detect 40% of patients who already have involved nodes: its "sensitivity" is low. However, we will recognize 80% of those patients who are free of node deposits by a normal lymphogram: fairly high "specificity". It follows that a normal lymphogram in a patient with prostatic carcinoma does not mean very much in our hands. This is because the false-negative rate, as the mirror image of our low true-positive rate, must be high (60%). But an abnormal lymphogram is likely to represent true node deposits because our fairly high true-negative rate must be matched by a low false-positive rate (20%) as its mirror image.

Table III shows how the lymphogram viewed in this way changes as more experienced observers are brought in. For those patients given unanimous judgements by the enlarged team, accuracy improves a little. The likelihood that the lymphogram will pick out the patient with deposits is 50% in these hands—still poor, with a corresponding 50% false-negative rate. The false-positive rate has improved, sinking to 15%.

Our findings are comparable with those of a similar study from Stanford University (Spellman *et al.*, 1977). We wish to emphasize that these studies involve node-by-node comparisons, not blanket statements of "lymphogram normal/abnormal" linked to overall histology assessments "nodes involved/clear". They point to serious defects in the prostatic carcinoma lymphogram for picking out the patient who already has lymph node involvement on presentation. However, if such deposits are diagnosed on lymphography, the likelihood of false-positive misdiagnosis is low.

As a parenthesis, we wish to add that we have given up pelvic lymphadenectomy, despite its apparent attraction as an accurate staging manoeuvre In this small series five patients suffered pulmonary embolism after the procedure, and this was fatal in one case. The problem of lymphatic staging in prostatic carcinoma remains wide open. Follow-up studies may increase the accuracy of lymphography (McIvor *et al.*, 1980).

Acknowledgments

We are grateful to many members of our prostatic carcinoma study group, including Professor G. D. Chisholm and our histopathologists Dr. R. C. B. Pugh and Dr. K. M.

Cameron. We also thank Dr. J. S. Macdonald and Dr. J. J. Stevenson (Royal Marsden Hospital) who kindly reviewed all the lymphograms (Table III).

REFERENCES

The Lancet, 1979. The value of diagnostic tests, *i*, 809–810.

McIvor, J., Massouh, H., Backhouse, B. M. and Macrae, K. D., 1980. Lymphography in prostatic carcinoma—implications for the diagnosis of metastases. *British Journal of Radiology*, *53*, 74–80.

McNeil, B. J., Keeler, E. and Adelstein, S. J., 1975. Primer on certain elements of medical decision making. *New England Journal of Medicine*, *293*, 211–215.

O'Donoghue, E. P. N., Shridhar, P., Sherwood, T., Williams, J. P. and Chisholm, G. D., 1976. Lymphography and pelvic lymphadenectomy in carcinoma of the prostate. *British Journal of Urology*, *48*, 689–696.

O'Donoghue, E. P. N., Constable, A. R., Sherwood, T., Stevenson, J. J. and Chisholm, G. D., 1978. Bone scanning and plasma phosphatases in carcinoma of the prostate. *British Journal of Urology*, *50*, 172–177.

Spellman, M. C., Castellino, R. A., Ray, G. R., Pistenma, D. A. and Bagshaw, M. A., 1977. An evaluation of lymphography in localized carcinoma of the prostate. *Radiology*, *125*, 637–644.

Book reviews

L'Urographie intraveineuse. Les Clefs de l'Interprétation. By J. F. Moreau and J. Affre. pp. 211. 1979 (Flammarion, Paris), 140 Fr.
ISBN 2-257-10264-9

In Britain uroradiologists are not numerous but in France there is a considerable body of radiologists with a major interest in the urinary tract and the Necker Hospital is one of the best known for this work. The two authors of this book are on the staff of this hospital and have set out to discuss intravenous urography partly from the stand-point of technique, but mainly in relation to interpretation. It is a slim volume of about 200 pages and is enriched with numerous diagrams by Martine Netter. These are quite remarkable. They are used partly to illustrate concepts, for example, how a calix alters its appearance with differing projection, but they are also used to replace radiographic images. The collaboration between authors with a clear idea of what they want to show and an able artist has resulted in the paradox of a profusely illustrated radiological textbook with very few radiographs. Because of this the book is not too difficult to follow for anyone with average French. It is, furthermore, divided into short paragraphs by numerous sub-headings and there are many "lists", *e.g.* causes of unilateral small kidney. The style is economical and rather dogmatic with an emphasis on a careful analysis of every film. This is, of course, something with which we all agree in principle but which is, surely, only part of the story of good interpretation. Too rigid an approach to each and every film may prevent the imaginative leap conceiving a diagnostic possibility which may then be confirmed from the films or by some further manoeuvre. Thus, although I do not disagree with the value of careful scrutiny of films, I would hesitate to say that this was the only route to satisfactory diagnosis. This comment apart, the book is a crisp, well-illustrated and useful introduction to the radiology of the urinary tract.

H. M. Saxton.

Dacryocystography. An Atlas and Textbook. By V. Gullotta and H. V. Denffer. pp. viii+68. 1980 (Georg Thieme Verlag, Stuttgart/New York; Thieme-Stratton Inc., New York), DM.58.
ISBN 3-13-5829014

This small book is presented excellently, with beautiful illustrations. The radiographs are lucidly demonstrated by the black line drawings accompanying them, and the explanatory legends. These illustrations are ample proof of the excellence of the technique the authors describe of simultaneous catheterization and injection of both canaliculi during fluoroscopy and with spot films during the procedure.

Open to criticism is the interpretation of the supposed pathology demonstrated by a distension technique in a physiological drainage system. Fig. 15 of a normal dacryocystogram could be interpreted as demonstrating an incomplete area of obstruction below the tear sac in the presence of epiphora.

Sufficient emphasis is missing concerning the correlation between the radiological and clinical findings, and the value of syringing prior to radiography.

Their table of advantages and disadvantages of the current techniques is biased in favour of their own method using microcatheters. It is, for example, untrue to say that macrodacryocystography inevitably produces some degree of blurring. The conventional technique, and macrodacryocystography, still have a very important role to play in the investigation of epiphora, and are usually associated with less radiation than fluoroscopy and spot films.

This book is well worth a place on the library shelf. When it is revised it would be nice to see the English edition improved by eliminating the constant use of the split infinitive.

W. Campbell.

1981, *British Journal of Radiology*, *54*, 18–23

Assessment of progression of secondary bone lesions following cancer of the breast or prostate using serial radionuclide imaging

By B. R. Condon, B.Sc., M.Sc.*, R. Buchanan, M.R.C.P., F.R.C.R., F.F.R.†,
N. W. Garvie, M.Sc., M.R.C.P., F.R.C.R.‡, D. M. Ackery, M.A., M.B., M.Sc.*,
J. Fleming, B.Sc., Ph.D.*, D. Taylor, M.Sc.*, D. Hawkes, B.A., M.Sc.* and
B. A. Goddard, Ph.D., F.Inst.P.*

*Department of Nuclear Medicine, Southampton General Hospital, Tremona Road, Southampton, Hampshire
†Wessex Radiotherapy Centre, Royal South Hants Hospital, Lyon Street, Southampton
‡Abteilung Radiologie III (Nuklearmedizin), Universität Ulm, D-7900 Ulm/Donau, Steinhovelstrasse 9, FRG

(Received March 1980 and in revised form August 1980)

ABSTRACT

A serial study on 32 patients with bone metastases following cancer of the breast or prostate was performed over three years. Up to ten sets of images (average of four) per patient were obtained during this period using ^{99}Tc^{m} methylene diphosphonate as the radiopharmaceutical. Ninety-three paired serial images of individual lesions were qualitatively assessed for change by three physicians in nuclear medicine and the results were compared with the quantitative results from computer analysis. The reproducibility of the quantitative approach was determined by the analysis of 20 paired lesions by three physicists. It was found that quantitative changes in uptake of less than 20% between images were generally not detected by the medical observers; a change of 41% had only a 95% probability of being identified as change by the physicians. Although much more reproducible in determining changes in individual lesions, the quantitative approach was found to be inferior to the qualitative assessment of overall change in the majority of cases which involve multiple lesions.

The basic assumption that uptake varies proportionally with progression of the bone lesion is discussed and is considered in some instances to be untenable. The conclusion is drawn that the determination of progression from changes of uptake in longstanding lesions is uncertain and is subsidiary in importance to the detection of new lesions.

The qualitative or "eyeball" assessment of serial radionuclide bone images by trained medical personnel has been used for some years to monitor the progression of secondary bone lesions following cancer of the breast or prostate (Galasko and Doyle, 1972). The digitization of these images and their transfer to computer for quantitative analysis is a more recent development (Citrin *et al.*, 1974) and various refinements have been introduced (Lurye *et al.*, 1977).

Radionuclide bone imaging is without doubt the most specific early indicator of metastatic skeletal involvement (Pendergrass *et al.*, 1973) but its performance in evaluating subsequent progression has not been adequately demonstrated. This paper is an attempt to provide a realistic evaluation of the qualitative and quantitative assessments of progression of disease.

MATERIALS AND METHODS

Thirty-two patients suffering from secondary bone lesions following cancer of the breast or prostate were serially imaged over a three year period. Up to ten sets of images (average of four) were obtained from each patient during this period using 550 MBq (15 mCi) of ^{99}Tc^{m} MDP (methylene diphosphonate) as the radiopharmaceutical. An interval greater than two hours was allowed between intravenous injection and imaging by a Toshiba 401 gamma camera. Information from the camera was assessed in two ways.

1. Conventional analogue film images were obtained, care being taken to ensure that the film blackening over normal bone was, as near as possible, the same for each image irrespective of the time period separating the images. This was achieved by acquiring a constant information density (counts/cm^2) over a region of normal bone.

2. The output of the camera was digitized (64×64 matrix) and transferred for storage onto a Medical Data Systems Trinary nuclear medicine computer system.

To evaluate the reproducibility of the qualitative assessment of changes in serial images, three experienced physicians in nuclear medicine compared pairs of serial scans of 93 lesions and were asked to score improvement or deterioration of each lesion accordingly to the scale in Table I. The progression of the lesions was assessed in quantitative terms using equation 1, which gives the percentage change in uptake between one scan and the next (the lesion uptake in the initial image being regarded as 100%).

$$\%\text{ change in uptake} = 100\left(\frac{C_{a2}/C_{n2}}{C_{a1}/C_{n1}} - 1\right) \quad . \ (1)$$

where C_a is the number of counts in the abnormal region, C_n is the number of counts in the normal

TABLE I

QUALITATIVE EVALUATION OF CHANGES OF UPTAKE IN INDIVIDUAL LESIONS—SCORING SCALE

	Score
Marked improvement	+2
Some improvement	+1
No change	0
Some deterioration	−1
Marked deterioration	−2

TABLE II

REPRODUCIBILITY OF QUANTITATIVE ANALYSIS

Method	95% confidence limits of agreement in terms of uptake
Contralateral (for SI joints and femoral heads)	8%
Profiles (spine)	8%
Profiles (skull)	16%
Contralateral (ribs)	> 20%

Uptake percentages calculated from equation 1.

TABLE III

QUALITATIVE ANALYSIS (93 LESIONS)

Comparison	Score differences				LWDS
	0	1	2	3	
A+B	52	36	5	0	46
A+C	60	32	1	0	34
B+C	50	40	3	0	46

A, B, C: Medical observers.
LWDS: Linear weighted difference scores.

region, 1 and 2 refer to successive scans and all regions are the same size.

Comparison regions of normal bone (Castronovo *et al.*, 1973) were chosen in each image to allow for scan-to-scan variations in renal function, dose of radionuclide and sensitivity of the camera. In the case of lesions in a sacroiliac joint, ilium or femoral head, the normal region chosen was the contralateral part of the anatomy. For spinal lesions a band about 6 cm wide was placed along the spine and the count profile obtained. The total counts over the lesion were calculated and a sloping background correction was applied using the counts in the two adjacent regions of normal bone.

To test the reproducibility of the quantitative approach, three physicists analysed paired serial scans of 20 individual lesions to determine the inter-observer variation.

RESULTS

The results from the study of inter-observer reproducibility in the quantitative analysis are given in Table II. The table shows, for example, that two physicists would agree on the uptake change in a spinal lesion to within 8% on 95% of occasions. It can be seen that reproducibility varies depending on the part of the skeleton analysed but is generally very good. Rib lesions are difficult to quantify because of their low count rate and because it is difficult to isolate the exact contralateral normal bone region. Skull lesions, provided that they do not cross the mid-line, can be quantified with a fair degree of precision using horizontal profiling techniques.

Uptake changes were assessed qualitatively using the score system detailed in Table I. The results from the analysis using this system are given in Table III and represent the scoring differences between two of the three physicians (A, B, or C) for each of the paired serial images of 93 lesions. A difference in score of zero indicates exact agreement which occurs, on average, 58% of the time. Differences of 1 are found 36% of the time and would occur, for example, if one clinician considered the lesion to be unchanged whilst the other considered it to have undergone some deterioration. In 3% of the cases marked differences of 2 were found in the score (the difference for example, between no change and marked deterioration). The measure of correlation used was the Linear Weighted Difference Score (LWDS). This arbitrary parameter is simply the sum of the number of differences in score multiplied by the value of the difference (*e.g.* for A+B, $\text{LWDS}=(52\times 0)+(36\times 1)+(5\times 2)+(0\times 3)=46$). The higher the LWDS, the lower the correlation.

An attempt was made to correlate the percentage uptake changes, measured by the quantitative analysis, with the scores determined by the qualitative analysis. Different levels of percentage change were equated with the scores and the quantitative results were then re-analysed in terms of the score system. The percentage levels which produced the minimum LWDS were the ones that correlated best with the qualitative analysis. The scores and the corresponding percentage changes are given in Table IV. The comparisons between the quantitative results (Q) and each of the physicians are given in Table V. From these last two tables it can be seen that, generally, a change of less than 20% in uptake is not identified as change by the physicians. Changes of 20–40% were generally regarded as

TABLE IV

BEST CORRELATION OF QUALITATIVE AND QUANTITATIVE RESULTS

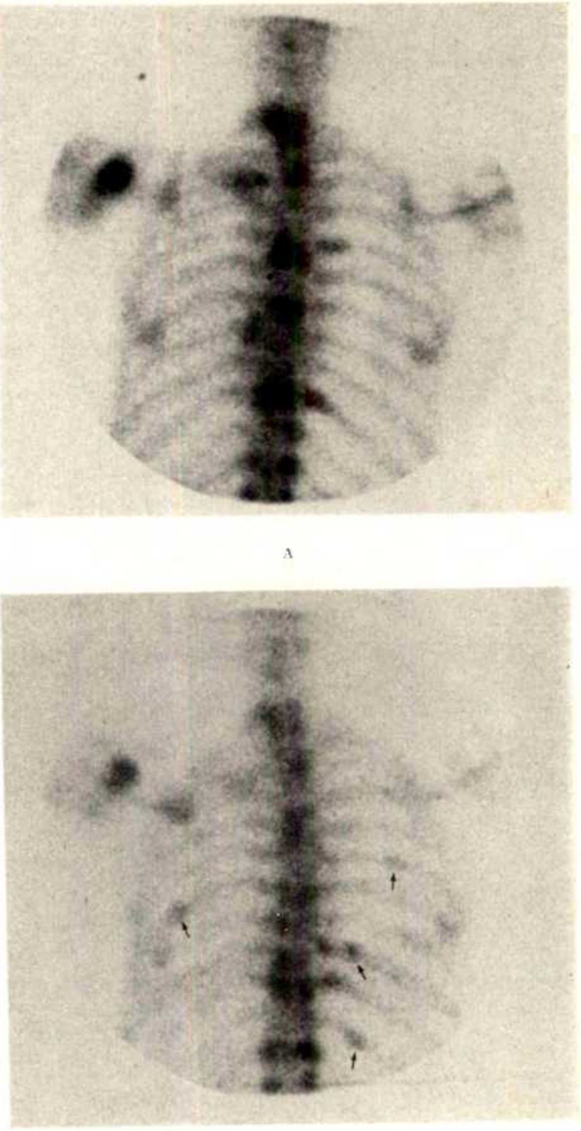
Scale	Meaning	% change
+2	Marked improvement	⩽ −40%
+1	Some improvement	−20% to −39%
0	No change	−19% to +19%
−1	Some deterioration	20% to −39%
−2	Marked deterioration	⩾40%

TABLE V

QUANTITATIVE AND QUALITATIVE COMPARISONS (93 LESIONS)

Comparison	Score differences				LWDS
	0	1	2	3	
Q+A	65	23	5	0	33
Q+B	49	40	4	0	48
Q+C	50	39	4	0	47

A, B, C: Medical observers.
Q: Quantitative analysis.


A

B

FIG. 1.

Metastases following Ca. breast (eight months' separation between scans). Decreased uptake in spinal lesions but new lesions in ribs.

"some change" and of over 40% as "marked change". Further analysis shows, however, that an uptake change of 41% has only a 95% chance of being identified as "change" by a trained medical observer.

In 36% of the lesions studied the clinicians disagreed by a score difference of 1, or about 20% change. Quantitative analysis is shown in Table II to be reproducible to within 10% at the 95% confidence limits for the spine and pelvis. The quantitative analysis is thus far more reproducible in determining uptake changes in individual lesions than the qualitative analysis.

DISCUSSION

It is often assumed that increasing uptake in a bone lesion implies progression. It is worth considering how valid this assumption is. Galasko and Doyle (1972) imaged 30 patients before and after treatment for cancer of the breast (three to four month interval) using fluorine 18 as the radiopharmaceutical. They expressed the view that avidity for the radionuclide and progression were related for both the "osteoblastic" and "osteolytic" types of lesion. They also expressed the view that the loss of avidity for the isotope by both types of skeletal mestastases indicated healing. We feel that the true situation is more complex than they suggest and that decreasing uptake may, in some cases, indicate progression. Our views have been partially engendered by the following observations based on the qualitative analysis of over 3000 bone scans.

1. Quite commonly there may be a general decrease in uptake in longstanding bone lesions but new lesions may still be appearing. Figure 1 shows two serial images (eight months' separation) with generally decreasing uptake in the spinal lesions with the appearance in the second radiograph of new rib lesions.

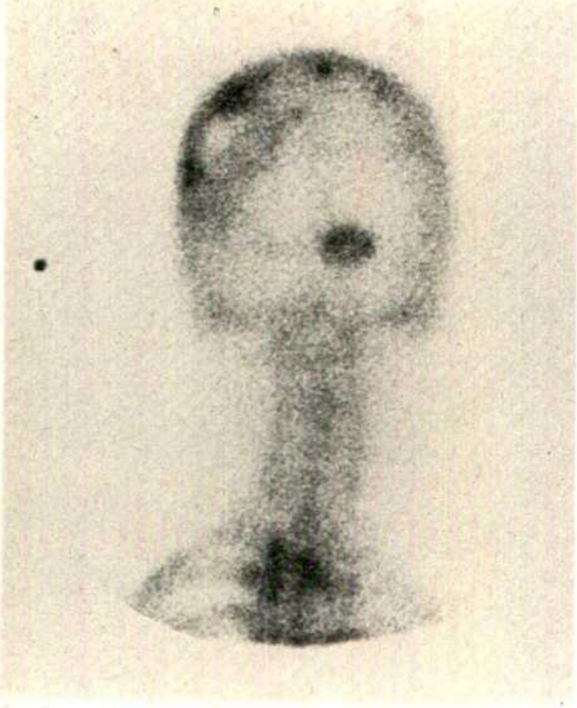


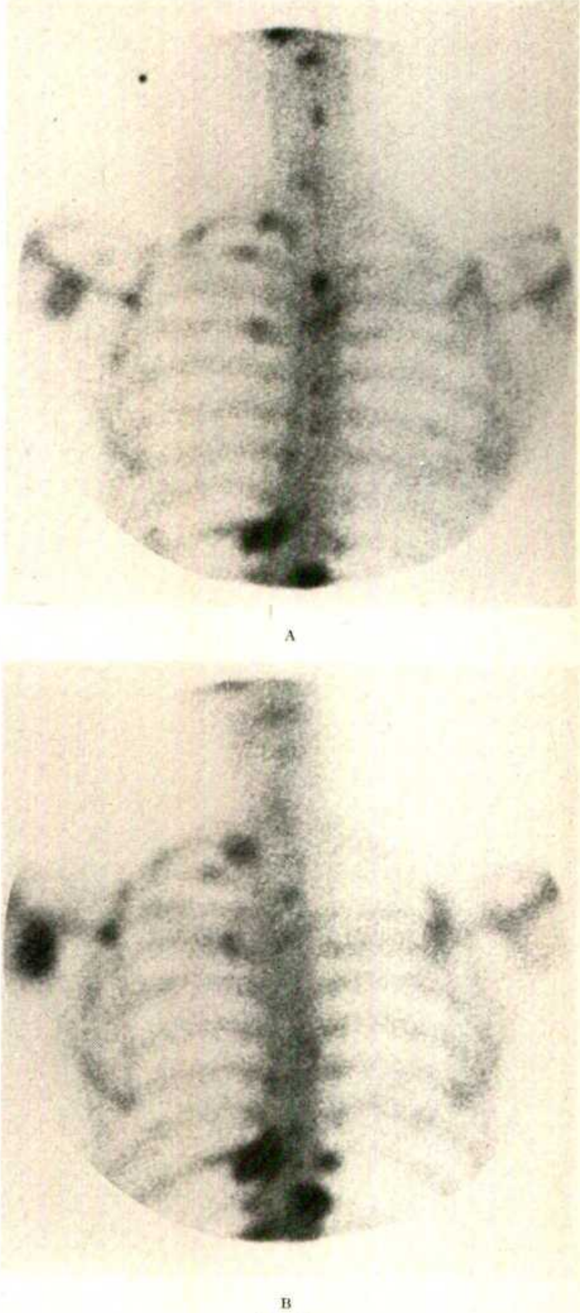
FIG. 2.
Metastases following Ca. breast. Penetration through cortex of bone leading to an apparently "cold" lesion.

2. Some lesions are so aggressive that they actually penetrate through the cortex of the bone, and the lesions appear to grow "cold" despite obvious tumour progression. An example of this is shown in Fig. 2.

3. Quite commonly, even in the case of a non-specific therapy, some lesions will decrease in uptake while others simultaneously increase in uptake. Figure 3 shows this with the cervical lesions decreasing in uptake whilst the T1 lesion increases markedly.

To try and understand these observations it is worth considering the nature of the lesions.

It is accepted that different kinds of secondary bone lesion react with the bone in different ways (Sutton, 1975). In the case of the purely "osteoblastic" type of lesion, which makes up the great majority of bone lesions following cancer of the prostate and about 10% of the lesions following cancer of the breast, it may be reasonable to assume that the response of the local osteogenic tissue is proportional to the progression of the tumour. The osteogenesis will occur, for the most part, at the interface between normal bone and lesion and so the uptake will be proportional to the surface area of the lesions.



A

B

FIG. 3.
Metastases following Ca. breast (two months' separation). Decreased uptake in cervical lesions but increased in T1 lesion.

Thus in the case of lesions with approximately spherical symmetry (surface area $\simeq 4\pi r^2$), uptake will not be linearly proportional to the lesion diameter, the quantity usually taken to express lesion "size", but to the square of the diameter.

In the case of the radiologically "osteolytic" type of lesion, which makes up most of the bone lesions following cancer of the breast and some from cancer of the prostate, it is unlikely that even a proportional relationship exists. Such aggressive lytic lesions may appear to suppress to a varying degree the "osteoblastic" response of the bone on the normal bone/lesion interface. The more aggresive the lesion, the faster it will destroy the bone, and so the greater the reduction in normal bone turnover in that area. The more aggresive the lesion, the less uptake will increase. It appears, from the relatively small percentage of false negative bone scans, that in the case of metastases following cancer of the breast or prostate the "osteolytic" aspects of the lesions do not totally dominate the "osteoblastic" response. Thus the presence of an "osteolytic" lesion can still be detected by increased uptake at a fairly early stage. To attempt to judge if the lesion is progressing after that point by changes in uptake will not, however, provide such an easily determined answer. It is for this reason that we feel that far more importance should be attached to the appearance of new lesions than to changes in uptake in previously existing lesions.

There are two other instances in which uptake and progression may not be linearly related.

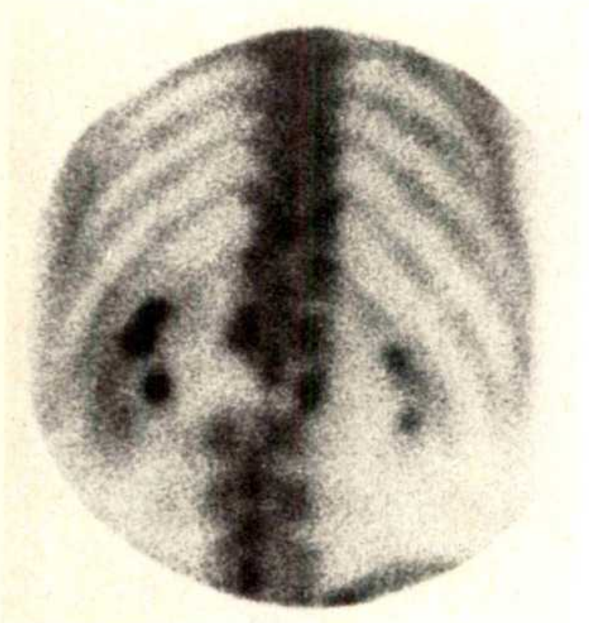


Fig. 4.

Destructive bone lesion in lumb arspine following Ca. bladder.

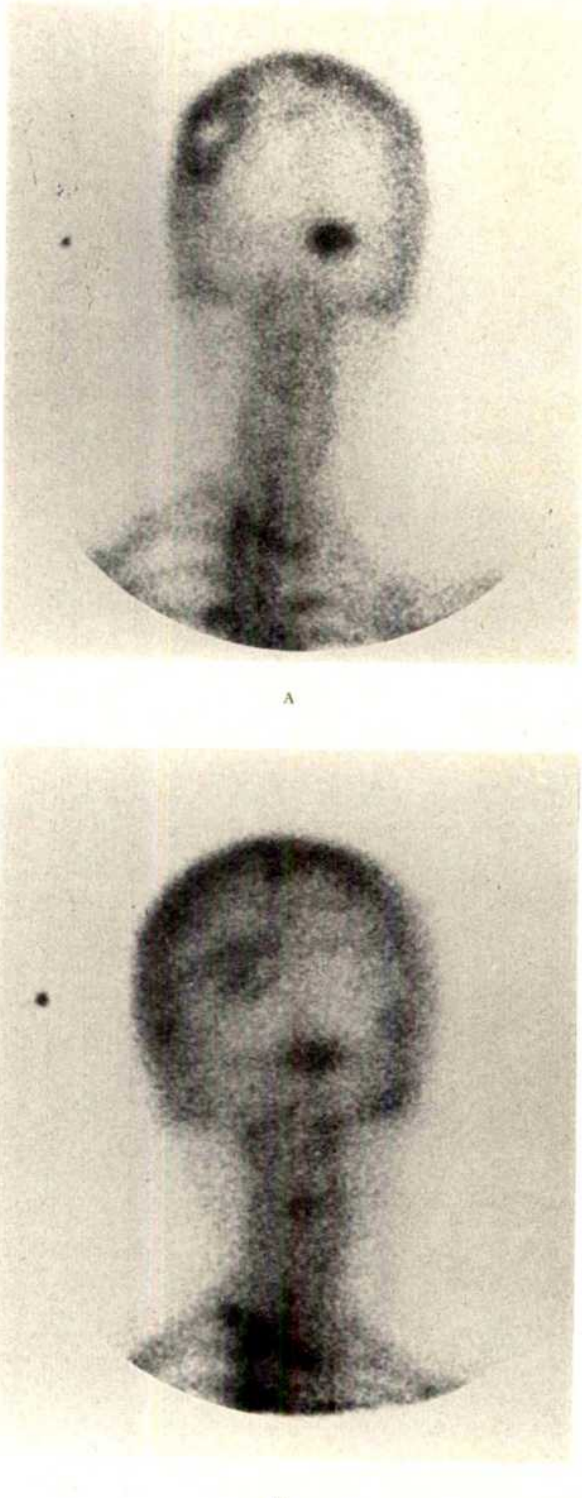


Fig. 5.

New bone formation following loss of lytic dominance (ten months' separation).

1. In some cases the lesion may penetrate through the cortex of the bone (Fig. 2), destroy the normal bone necessary to provide an osteoblastic response, and will appear to grow "colder" at these points. The more the lesion progresses the larger it will grow and so the colder it will get. Although such lesions may be recognized for what they are in the skull or other flat bones they may not be so obvious in the more complex structure of the vertebra until very far advanced (Fig. 4). The lesion is progressing but the uptake is not increasing.
2. When an osteolytic lesion regresses new bone is formed, either because of the osteoblastic response to the presence of the lesion or because the bone is actually attempting to repair itself. If the latter explanation is the case then the uptake would increase but the tumour would have regressed and the bone would be healing (Fig. 5).

Although quantification is far more precise than the qualitative approach for determining changes in uptake in individual lesions, it is for the above reasons that we feel that the qualitative assessment by trained medical personnel is more representative of overall progression of disease. This is especially true in the most common cases of patients with multiple metastases. In these cases many of the lesions may be badly positioned for quantification, with some lesions increasing in uptake while others are decreasing in uptake and new lesions are appearing. Quantitative analysis of a few selected lesions is unlikely to be representative of the overall change in uptake, which is itself not necessarily representative of the progression of the disease.

CONCLUSIONS

Quantitative analysis is far more precise than qualitative assessment for analysing changes in uptake in individual lesions but is inferior to the qualitative assessment of disease progression in the most common cases of patients with multiple metastases.

Changes in uptake of up to 41% are required before a change is recognized with 95% confidence by trained medical personnel. Changes in uptake of less than 20% are generally not recognized.

Increased uptake is not necessarily proportional to progression. More significance should be given to the appearance of new lesions rather than increased uptake in old ones.

REFERENCES

CASTRONOVO, F. P., POTSAID, M. S. and PENDERGRASS, H. P., 1973. Effects of radiation therapy on bone lesions as measured by $^{99}\mathrm{Tc}^{\mathrm{m}}$–diphosphonate. *Journal of Nuclear Medicine*, *14*, 604–605.

CITRIN, D. L., BESSENT, R. G., TUCHY, J. B., GREIG, W. R. and BLUMGART, L. H., 1974. Quantitative bone scanning: a method for assessing response of bone metastases to treatment. *Lancet*, *i*, 1132–1133.

GALASKO, C. S. B. and DOYLE, F. H., 1972. The response to therapy of skeletal metastases from mammary cancer. Assessment by scintigraphy. *British Journal of Surgery*, *59*, 85–88.

LURYE, D. R., CASTRONOVO, F. P. and POTSAID, M. S., 1977. An improved method for quantitative bone scanning. *Diagnostic Nuclear Medicine*, *18*, 1069–1073.

PENDERGRASS, H. P., POTSAID, M. S. and CASTRONOVO, F. P., 1973. The clinical use of $^{99}\mathrm{Tc}^{\mathrm{m}}$–disphosphonate (HEDSPA). A new agent for skeletal imaging. *Radiology*, *107*, 557–562.

SUTTON, D., 1975. *Textbook of Radiology* (2nd edition). (Churchill-Livingstone, Edinburgh), pp. 112–114.

Book review

Clinical Cardiac Radiology. By Keith Jefferson and Simon Rees. 2nd ed. pp. xii + 300, 1980 (Butterworth, Sevenoaks), £35·00.
ISBN 0-407-13576-6

This book is primarily on the plain chest X-ray appearances of heart disease. It is particularly good in the area of the authors' greatest experience, in those relatively common conditions which survive beyond infancy, and here the authors' great personal knowledge shines through. Throughout the text the chest X-ray appearances and the derangement of function are skilfully correlated on the basis of this experience.

In its attempt to be comprehensive the pathological anatomy not only of common conditions but also of the relative rareties is extensively described, though without many illustrations. The modern (and rather obscure) terminology is used which might make it heavy going for the occasional reader.

I do not feel that the increase in the number of angiocardiograms in this edition has been helpful. Those which serve to illustrate the basis of the plain film appearance are excellent but a large number are included to illustrate the angiographic appearances of the conditions described. They are largely unannotated and therefore unhelpful for the neophyte and superfluous for the expert.

This remains one of the best books available on the plain chest X-ray appearances of heart disease.

M. J. RAPHAEL.

1981, *British Journal of Radiology*, *54*, 24–28

A physical assessment of the imaging performance of a panel-type X-ray image intensifier

By G. A. Hay, M.Sc. and A. R. Cowen, B.Sc.

Department of Medical Physics, University of Leeds, The General Infirmary, Leeds LS1 3EX

(*Received March 1980 and in revised form August 1980*)

Abstract

The performance of a commercial panel-type X-ray image intensifier has been investigated by physical methods, both objective and subjective. The objective measurements show that the manufacturer's claims are justified, except perhaps in regard to contrast loss. The subjective measurements reveal that the conversion factor ("gain") of the device is such that dark-adaptation is not necessary, though best results are obtained in a nearly dark room. Hence the device confers a significant advantage, both in information and in dose to the patient, over traditional fluoroscopy. However, the conversion factor is nearly three orders of magnitude smaller than that of a conventional X-ray image-intensifier television system. Therefore, at modern fluoroscopic exposure rates, the eye is operating at light levels at which its own deficiencies set a limit to the perceptible information. To equal the performance of modern fluoroscopy the exposure rate to the intensifier must be increased to about 20 times the value customary in modern fluoroscopy. This can be done only by increasing the X-ray factors (kV and mA), resulting in a corresponding increase in dose to the patient of about one order of magnitude. Such an increase is in many circumstances unacceptable.

A panel intensifier makes use of conventional X-ray image-intensifier techniques, except that the input and output screens are of equal size and spaced apart by a small distance of the order of 10 mm (Wang *et al.*, 1977). The present intensifier was manufactured by Diagnostic Information Inc. and marketed by Oldelft (UK) Ltd. It has an effective operating area of about 180 mm square with the corners cut off. The input screen is of evaporated caesium iodide (sodium activated), and the output screen of zinc–cadmium sulphide. A lead glass protective screen is permanently fitted to the output for the protection of the radiologist, as in traditional fluoroscopic techniques. A potential difference of the order of 50 kV, produced by an internal transistorized power unit, is maintained between the thin aluminium coating of the output screen and the photocathode, as in conventional image-intensifier design. However, because the output screen is of the same size as the input screen, no gain in luminance can arise from area minification, the only gain being due to the increase in electron energy. This fact severely limits the overall conversion efficiency of the device (by a factor of 100 or so).

Objective Measurements

Conversion factor

The conversion factor was measured by placing the intensifier in the beam from a calibrated half-wave rectified X-ray generator with no cables (a dental set) operating at 70 kVp. The luminance at the centre of the screen was measured using a photometer with photopic response (Model 700 Log-linear Photometer, Gamma Scientific, Inc., San Diego, California) that had been calibrated against a standard light source (Model 220–1 C, Luminance Standard Head, Gamma Scientific, Inc.). The conversion factor was found to be 2.57 cd m^{-2} per mR s^{-1}, instead of the claimed 3.05 cd m^{-2} per mR s^{-1} (non-SI units are used here and on subsequent occasions because this is a widely-accepted international standard of conversion factor). This compares with conversion factors of conventional image intensifiers of 50 to 150 cd m^{-2} per mR s^{-1}, in addition to which a television system will give a gain of five to ten times. The e.h.t. adjustment in the intensifier was set to the value recommended by the manufacturer. Higher values of conversion factor could undoubtedly have been achieved by increasing this value, but only at the expense of electrical stability.

Contrast loss

The contrast loss was first measured by the method recommended by the manufacturer, currently widely used. First, the whole screen was irradiated with X rays and the central luminance measured. Second, a circular lead stop (2 mm thick, 57 mm diameter), equal in area to one-tenth of the total screen area, was placed in the X-ray beam at the centre of the field, and the central luminance again measured. Assuming zero contrast loss, the luminance behind the lead stop should be zero. Owing to scatter of light and lateral diffusion of electrons it is not, and the ratio of the luminance without the stop to the luminance with the stop is generally called the "contrast ratio". The larger the contrast ratio, the smaller is the contrast loss. We obtained a value of 10.5:1, instead of the manufacturer's claim of 9.8:1. This value is also typical of an average modern X-ray image intensifier of conventional design. However, we have grave doubts as to the significance of this value in relation to true contrast loss, because so much depends on the extent and distribution of the "skirts" of the line spread-function. Our subjective impression is that the panel intensifier is significantly worse than a conventional X-ray image-intensifier system in this respect.

Accordingly, we attempted to make a comparative assessment of contrast loss by another method. A copper and lead step-wedge of calibrated transmittance in steps of 0.1 (Leeds test object type GS 1) was placed in the field, and the luminance produced by the intensifier behind each step of the wedge was measured. This measurement had already been done for a modern conventional X-ray image-intensifier television system of good performance (including the monitor), and a comparison between the two is shown in Fig. 1. For a step-wedge transmittance of effectively zero, when the screen should be black, the television system shows a luminance due to scattered light etc. of only 8% of peak white, whereas the panel intensifier reveals no less than 28% (the dimensions of the opaque section of the step wedge were 20 × 10 mm). Though this is an empirical test, and has no fundamental significance, the result confirms our subjective impression of rather serious contrast loss. Of course, it can be argued that the luminance of the television monitor could be manipulated to any desired value by altering the "brightness" control. However, in our measurements, the monitor is carefully set by objective methods so that black-level input yields a nearly-zero luminance (in fact, 0.16 cd m^{-2}, 0.05 ft L).

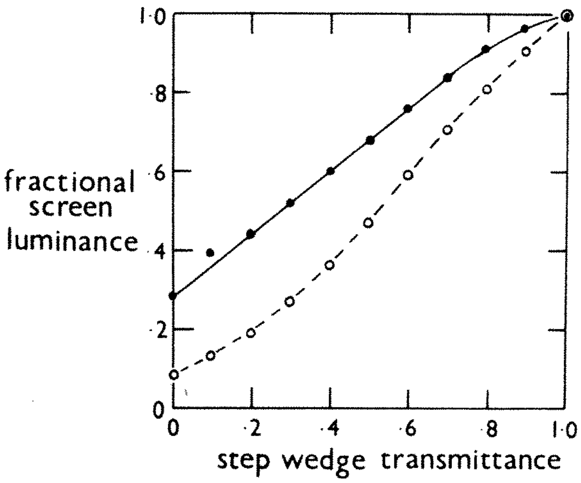


FIG. 1.

Relative X-ray input (step-wedge transmittance) *vs.* relative light output (fractional screen luminance) of two systems: —●—●—●—●— the panel intensifier;—○—○—○—○— a conventional intensifier-television system, showing the greater contrast loss in the panel intensifier.

Modulation transfer function (*MTF*)

We should have liked to obtain a complete MTF by Fourier transformation of line and edge spread-functions, but the very thick layer of lead glass at the output face of the panel intensifier rendered our precision optical scanning devices useless. However, in view of the contrast loss measurements described above and the unequivocal conclusions drawn from the limiting resolution and other subjective measurements below, it is perhaps not so important to know the precise form of the MTF.

SUBJECTIVE MEASUREMENTS

Limiting resolution

The limiting resolution was measured using the above X-ray generator at 50 kVp (no filter), in conjunction with a Funk type 18 test object.* The test object consists of 21 groups of line pairs, each having 4½ cycles of a range of spatial frequency from 0.5 to 5.0 cycles mm^{-1}. (This test object, of course, does not quite measure "true" limiting resolution because of the square profile of its intensity distribution, because the contrast is not quite 1.00 and because there are only 4½ cycles in each frequency group). The limiting resolution was taken to be the average of that judged by two experienced observers (the authors). It was found to be 1.92 cycles mm^{-1}, instead of the claimed 1.88 cycles mm^{-1}. However, to attain this figure, the screen had to be viewed through a 5× magnifier, at a clinically unrealistic exposure rate of 61 μGy s^{-1} air kerma (7 mR s^{-1}), thus optimizing the effective resolution of the eye in relation to that of the intensifier. The above values of limiting resolution, however, are not available to the radiologist in clinical use, for two reasons. First, at more realistic exposure rates, the limiting resolution deteriorates because visual resolution itself is inferior at low light levels, probably because of the reduced quantum flux density of the light absorbed by the retina (van Meeteren and Vos, 1972). Second, without the magnifier, at more realistic viewing distances, the limiting resolution deteriorates because the detail in question subtends a much smaller angle at the eye. Figures 2 and 3 respectively show the deterioration in limiting resolution due to these two causes separately; the loss in performance is very significant. When both causes operate together, the loss is greater. For example, at a viewing distance of 250 mm and an exposure rate of 2.6 μGy min^{-1} air kerma (300 μR s^{-1}), probably realistic for the panel intensifier but very high for a conventional X-ray intensifier system, the measured limiting resolution was only 1.0 cycles mm^{-1}. At an exposure rate more acceptable to the patient of 0.26 μGy s^{-1} air kerma (30 μR s^{-1}), at which the screen image was very faint indeed, the estimated resolution was only 0.75 cycles mm^{-1}.

---

*(Funk Optik Foto GmbH, Am Hugenottenplatz, Postf. 1669, 8520 Erlangen, W. Germany).

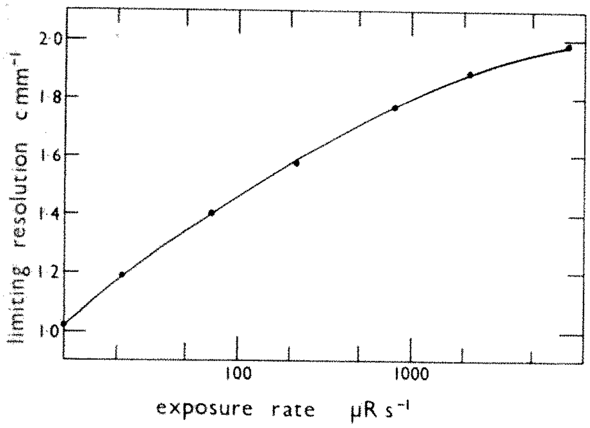


FIG. 2.

Limiting resolution of the panel intensifier (measured with a 5× magnifier) *vs.* input exposure rate, showing the deleterious effect of decreasing luminance.

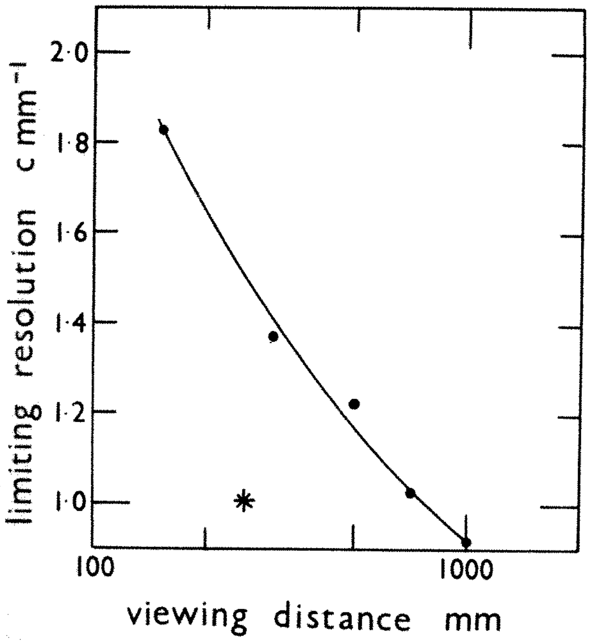


FIG. 3.

Limiting resolution of the panel intensifier *vs.* viewing distance at 61 μGy s^{-1} air kerma (7 mR s^{-1}). The asterisk shows the estimated resolution at 250 mm and 2.6 μGy s^{-1} (300 μR s^{-1}); the estimated resolution at 250 mm and 0.26 μGy s^{-1} (30 μR s^{-1}) is 0.75 cycles mm^{-1}.

Of course it can be claimed with reason that limiting resolution is not the only important imaging property of an intensifying system. However, the manufacturers claim (Wang *et al.*, 1977) a high value of limiting resolution and a good MTF; the fact that these are not in practice available to the radiologist, and the high degree of contrast loss, suggest that the performance of the panel intensifier will be inferior in clinical practice to that implied by the manufacturer's claims.

Geometry and uniformity of luminance

The geometry was investigated by viewing the image of a metal wire mesh of 2 cm spacing and 1 mm thickness (Leeds test object type M1); it was judged subjectively to be excellent. The uniformity of screen luminance was not measured objectively, but subjectively it appeared excellent and generally superior to conventional systems.

Low-contrast sensitivity

The visual detectability of large (11 mm) discs (Leeds test-object N1) placed close to the entrance plane of the intensifier was judged over a range of exposure rate of 87 nGy s^{-1} air kerma (10 μR s^{-1}) to 4.4 μGy s^{-1} (500 μR s^{-1}) using the same 70 kVp generator as before with a 1 mm copper filter; the contrasts of the discs were known accurately. (Contrast is here defined as the difference between the exposure rate behind the disc and the background exposure rate, divided by the background exposure rate.) Perceptibility was taken to be the average of

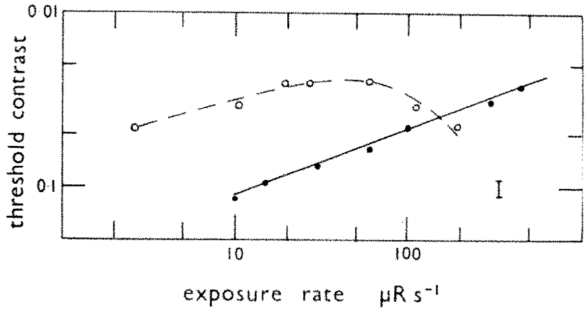


FIG. 4.

Threshold contrast *vs.* exposure rate for 11 mm diameter discs, for —●—●—●—●— the panel intensifier, and —O—O—O—O— a conventional intensifier–television system. The error bar indicates the uncertainty of the measurements.

that judged by two observers well accustomed to such measurements (the authors).

Figure 4 shows the threshold contrast as a function of exposure rate for the panel intensifier and also for a typical modern conventional image-intensifier–television system. Two significant conclusions may be drawn from this. First, at a typical exposure rate for modern fluoroscopy (0.26 μGy s^{-1} air kerma, 30 μR s^{-1}) the contrast sensitivity of the panel intensifier is about three times worse than that of the conventional system. Second, to equal the contrast sensitivity of the conventional system at this exposure rate, the exposure rate at the panel intensifier must be increased by a factor of no less than 20. This, of course, can be done in clinical practice only by increasing the X-ray factors (kV and mA); it will be accompanied by a corresponding increase in dose to the patient. Unfortunately, the magnitude of this increase cannot be simply calculated from the X-ray factors (kV and mA), for several reasons; for example, the complex effect of change of kV and the notorious inaccuracy of mA meters at low values of mA.

While performing this measurement, it was noticed that no X-ray quantum noise was perceptible at any exposure rate within the range tested. This observation was at first sight remarkable, until it was realized that it was a direct result of the relatively low conversion factor of the panel intensifier. For a conventional image-intensifier–television system, with an input exposure rate of 0.26 μGy s^{-1} air kerma (30 μR s^{-1}) and a monitor peak luminance of 48 cd m^{-2} (15 ft L), the overall conversion factor can be as much as 1500 cd m^{-2} per mR s^{-1}. This is to be compared with values of about 3 cd m^{-2} per mR s^{-1} for the panel intensifier, and about 0.01 cd m^{-2} per mR s^{-1} for traditional fluoroscopy. As a result, with the panel intensifier, the eye is operating at a much lower light level than it is with the television system, and the performance of the whole system (including the radiologist) is thus limited to a large extent by the limitations of the human eye at such light levels (despite the fact that dark adaptation is unnecessary). The situation is reminiscent of that obtaining in traditional fluoroscopy (Chamberlain, 1942; Sturm and Morgan, 1949); indeed, it will be shown below that the performance of the panel intensifier lies between that of traditional fluoroscopy and that of modern television fluoroscopy.

In contrast, it was noticed (though not mentioned above) that during the resolution measurements previously described, X-ray quantum noise was clearly perceptible at all exposure rates using the 5× magnifier. This is a direct result of increasing the effective numerical aperture of the pupil of the eye (by a large reduction in viewing distance) and hence increasing the effective quantum efficiency of the eye to the light flashes that are produced by the X-ray quantum interactions (Sturm and Morgan, 1949).

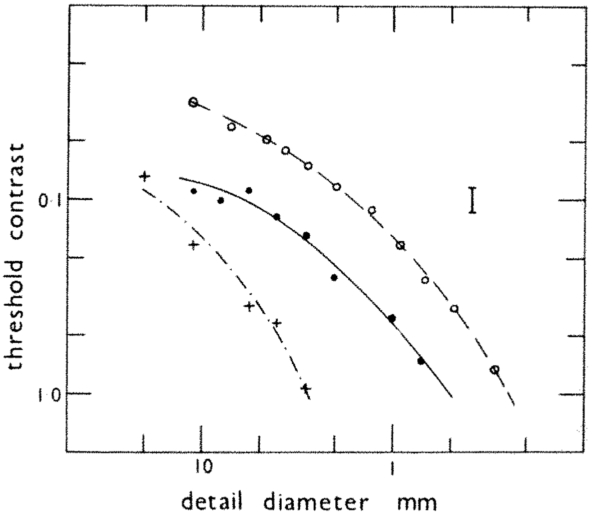


FIG. 5.

Threshold contrast *vs.* detail diameter at 0.26 μGy s^{-1} for three systems: —●—●—●—●— the panel intensifier, —O—O—O—O— a conventional intensifier–television system, and ·+·—·+·—·+·—·+·— traditional fluoroscopy. The error bar indicates the uncertainty of the measurements.

Threshold contrast detail diagrams

Figure 5 shows threshold contrast detail diagrams, using the "Leeds" test object type TO 5 (Hay, 1964), for a conventional system of good performance, for the panel intensifier and for traditional fluoroscopy, all at 0.26 μGy s^{-1} air kerma (30 μR s^{-1}). (Threshold contrast is the lowest value of X-ray contrast that is detectable in the given conditions.) The performance of the panel intensifier lies approximately mid-way between the two other systems (on logarithmic scales). This implies that the performance of the panel intensifier is significantly superior to that of traditional fluoroscopy; it thus offers a highly acceptable alternative to simple fluoroscopy in situations where money is short or where servicing facilities for the more complex systems are absent, for example in developing countries.

On the other hand, the performance of the panel intensifier is significantly inferior to that of a modern conventional image-intensifier system that is operating optimally; this leads to the undesirable consequences described above. By way of verification, Fig. 6 shows threshold-contrast detail diagrams for a conventional system at 0.26 μGy s^{-1} (30 μR s^{-1}) and

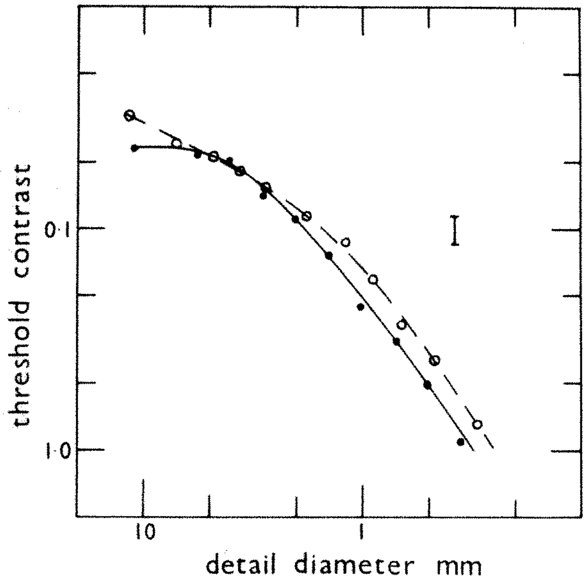


Fig. 6.

Threshold contrast *vs.* detail diameter for:—●—●—●—●— the panel intensifier at 2.6 μGy s^{-1} (300 μRs $^{-1}$), and —O—O—O—O— a conventional intensifier-television system at 0.26 μGy s^{-1} (30 μR s^{-1}). The error bar indicates the uncertainty of the measurements.

for the panel intensifier at 2.6 μGy s^{-1} (300 μR s^{-1}). The performance of the panel intensifier is nearly as good as that of the conventional system, but at the expense of operating at ten times the exposure rate. This further supports our previous conclusion that to attain equal performances an increase in exposure rate of about 20 times that of the conventional system is needed, leading to an unacceptable dose to the patient.

Lag

By visual inspection of the image of our lag test object, in which a disc of lead is moved rapidly (10^3 mm s^{-1}) over a distance of about 25 mm in the field of view, the lag of the panel intensifier was subjectively judged to be negligible. This is is accordance with the known fast response of both caesium iodide (the input screen of the intensifier) and zinc–cadmium sulphide (the output screen).

Conclusions

The panel intensifier represents a radical improvement over traditional fluoroscopy, in terms of both performance and dose to the patient. If its conversion factor ("gain") could be increased by an order of magnitude, without deterioration in its other properties, and if its contrast loss could be markedly improved, it could be regarded as a serious competitor to the conventional image-intensifier television system.

Acknowledgments

We acknowledge many helpful discussions with Mr. O. F. Clarke, of this department. Mr. N. J. Coleman made the test objects.

We thank Messrs. Oldelft (England) for the loan of the panel intensifier. The work was supported in part by a grant from the Department of Health and Social Security.

REFERENCES

Chamberlain, W. E., 1942. Fluoroscopes and fluoroscopy. *Radiology*, *38*, 383–413.

Hay, G. A., 1964. A physical assessment of the Cinelix electro-optical image intensifier in television fluoroscopy. *Radiology*, *83*, 86–91.

Meeteren, A. van and Vos, J. J., 1972. Resolution and contrast sensitivity at low luminances. *Vision Research*, *12*, 825–833.

Sturm, R. E. and Morgan, R. H., 1949. Screen intensification systems and their limitations. *American Journal of Roentgenology and Radium Therapy*, *62*, 617–634.

Wang, S. P., Robbins, C. D. and Bates, C. W., 1977. A novel proximity X-ray image intensifier tube. *Proceedings of the Society of Photo-optical Instrumentation Engineers*, *127*, 188–194.

1981, *British Journal of Radiology*, 54, 29–35 JANUARY 1981

Radiation myelopathy in patients treated for carcinoma of bronchus using a six fraction regime of radiotherapy

By S. Dische, M.D., F.R.C.R., W. M. C. Martin, M.R.C.P., F.R.C.R. and P. Anderson, B.Sc.

Marie Curie Research Wing, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

(Received March 1980 and in revised form July 1980)

ABSTRACT

The adoption of a six-fraction regime of radiotherapy for patients with locally advanced carcinoma of the bronchus was followed by the appearance of radiation myelitis in eight cases. These were among a group of 130 patients given radiotherapy with anterior and posterior treatment fields, without shielding of the spinal cord. Radiation myelitis was found only in those where the calculated spinal-cord dose exceeded 3350 cGy (rad).

The possible precipitating factors in the eight patients who suffered myelopathy were compared with those in the remaining 62 patients who also received spinal-cord doses calculated to be greater than 3350 cGy (rad). Only one difference was found—the haemoglobin concentration was significantly higher in those who suffered neuropathy compared with those who did not ($P = 0.05$).

Case reports concerning radiation damage to the spinal cord first appeared in the 1940's (Ahlbom, 1941; Smithers *et al.*, 1943; Stevenson and Eckhardt, 1945). Jones (1964) distinguished the separate transient and progressive types of radiation myelopathy each with their differing pathology and prognosis.

There has been general agreement that there is a rising incidence of myelopathy with radiation dose. Increasing fractionation and overall time appear to reduce the incidence of this complication (Dynes and Smedal, 1960; Wara *et al.*, 1975). Factors which may increase the incidence include the length of cord irradiated (Boden, 1948), hypertension (Asscher and Anson, 1962) and the use of hyperbaric oxygen (Coy and Dolman, 1971; Van den Brenk *et al.*, 1968).

At Mount Vernon Hospital one of the authors (SD) from September 1965 used a 20-fraction regime of radiotherapy over four weeks to a minimum tumour dose of 5000 R (4850 cGy) for the treatment of locally-advanced carcinoma of the bronchus. However, work with hyperbaric oxygen in a number of tumour sites using a six-fraction technique with a maximum tissue dose of 3600 R (3500 cGy) given over 18 days, pioneered by Churchill-Davidson *et al.* (1966), gave rise to an impression that this technique could also be employed for conventional radiotherapy in air. Thus from the end of 1970 a six-fraction technique was adopted as the standard for locally advanced carcinoma of bronchus. While the long-term benefit was possibly less satisfactory than with conventional multifraction radiotherapy or six fractions in hyperbaric oxygen, the immediate response seemed no different. Patients were found to tolerate the six-fraction technique relatively well. With attendance for treatment only twice weekly and for three weeks, the regime was convenient for the patients, reduced the burden on a busy department and seemed suitable for patients with carcinoma of the bronchus where, in most cases, immediate relief of symptoms was the most important objective. An occasional patient with a small tumour was still treated using the 20-fraction technique, but there were never more than three such patients per year.

One case of radiation myelopathy appeared among the patients treated with 20 fractions between 1965 and 1970. A further case presented in 1975 among those treated with the six-fraction technique, but when further cases were diagnosed in the subsequent two years it seemed possible that the technique was leading to an unduly high incidence of radiation damage to the spinal cord. A review of these patients was undertaken with special attention to the incidence of radiation myelitis.

MATERIALS AND METHODS

Between September 1965 and December 1976 about 1300 patients with carcinoma of bronchus were referred to the clinics held by one of the authors. Radiotherapy was advised in 854 of these patients. Nearly all received radiotherapy to the primary site and mediastinum including, in some cases, the lower cervical region.

In the cases of radiation myelitis observed, symptoms appeared at least eight months after initiation of radiotherapy. It was decided, therefore, to simplify the survey by examining the records only of those who had survived at least six months. This left a total of 303 cases or 36% of those who received any form of radiotherapy. The patient's case notes and treatment sheets were examined and where relevant those of the district hospitals were obtained.

It is our practice to follow up all patients who received radiotherapy as their definitive treatment for carcinoma of bronchus. Some cases were also seen during the later stages by colleagues in associated chest units and a number of patients received terminal care in chest unit wards—chest clinic records were all made freely available to us. All incidents in the follow-up period which could have been related to a radiation myelopathy were investigated as far as it was possible. Follow-up was considered adequate for patients who were alive if they had been seen in the radiotherapy and oncology clinic less than three months before the survey or, for patients who were dead, if they had been seen in the three months before death and there was some information as to the condition at the time of death. Forty-seven patients had to be excluded on the grounds of inadequate follow-up (Table I).

The patients with the smallest areas requiring treatment and who were generally fit and well were considered to have the best prognosis and received treatment with an anterior field and a postero-lateral one with the beam modified by a wedge filter. This arrangement was designed so as to avoid including the spinal cord in the high-dose area. After 1970 the number of cases selected for this plan became small. In all there were 38 such patients and these have also been excluded from the analysis, as have 17 patients with advanced disease given palliative therapy using an anterior field alone. This, therefore, left a total of 201 patients treated with opposed fields, anterior and posterior. In none of these patients was the spinal cord shielded. This policy not to employ cord shielding was influenced by the long experience of Cade and McEwen at Portsmouth where in over 300 patients treated in six fractions with opposed fields, either in hyperbaric oxygen or in air, no case of radiation myelopathy had been reported (Cade and McEwen, 1978).

TABLE I

Case material

Patients with carcinoma of bronchus treated by radiotherapy		854
Patients surviving over six months		303
Exclusions:		
Inadequate follow-up	47	
Treated by single field	17	
Planned to avoid spinal cord	38	
Insufficient data to estimate cord dose	18	
Total excluded	120	
Total number treated by opposing fields, no spinal cord shielding, cord dose known:		183
Number treated in 19–21 fractions	22	
Number treated in 6 fractions	130	
Number treated by other fractionation	31	
	183	

From September 1965 until July 1971 patients were treated either on a 4 MV linear accelerator or on a cobalt unit operating at 75 cm source-skin distance. At that time two cobalt units operating at 90 cm SSD were introduced and until December 1973 most of the patients were treated on these units. In December 1973 a new 8 MV linear accelerator, replacing the 4 MV unit, became operational. Since that time the majority of the patients have been treated on that machine with just an occasional patient receiving treatment on one of the cobalt units.

From September 1965 until October 1970 a 20-fraction course of radiotherapy with daily treatments from Monday to Friday to a minimum tumour dose of 4850 cGy (rad) was standard. The six-fraction technique was introduced in November 1970 and until November 1973 a mid-plane, mid-line dose of 3000 cGy was employed. As all seemed satisfactory the dose was then increased and the patients were treated to a maximum dose of 3500 cGy. It was felt that the measurement of a "maximum" dose allowed the greatest dose to be given to the tumour whilst safeguarding the normal tissues, especially in those patients where the distance between front and back skin surfaces was large in whom mid-plane doses were considerably lower than those in the subcutaneous tissues. However, the dose was reduced by 10 to 15% in patients whose disease was so advanced that the area to be irradiated was greater than 180 cm^2 viewed in the antero-postero direction or when there was an impairment of general condition by reason of co-existing disease or age.

A pro-forma was prepared for gathering of data relating to the patients. These included details of the radiotherapy such as dose, fractionation, overall time, date of commencement, apparatus employed, the field arrangement, use of any sensitizing method, the status of the patient at the date of last follow-up or death, and information which might be relevant to the incidence of myelopathy, viz. the site and histology of the tumour, the age and sex of the patient and the blood pressure and haemoglobin concentration at the time of treatment.

The data were entered into the departmental computer. Following the work of Brinkley and Masters (1967), the spinal cord was taken in all cases to be 5.0 cm from the posterior skin surface, and using appropriate depth dose data for the machine and the field sizes employed the spinal cord dose was calculated. In a further 18 cases insufficient data were available for calculation of the cord dose and so these had to be excluded from some of the analyses.

The neurological findings in these patients were carefully reviewed. The diagnosis of radiation myelitis was based upon symptoms and signs indicating cord damage at a level within the field of radiotherapy and a myelogram showing no other abnormality.

RESULTS

The diagnosis of radiation myelopathy was established in nine patients. All were of the progressive and none of the transient type (Table II). One received radiotherapy in 1967 during the period when 20 fractions were employed. At that time it was common practice for only one field of an opposed pair to be treated on each treatment day. Furthermore, at the beginning of treatment the anterior field was treated consecutively while check films were taken and minor alterations made. The posterior field was then treated on two consecutive days. The cord dose in this case was estimated to be 4977 cGy which in 20 fractions spread over the 29 days gives a TDF of 90.9. Because of the manner in which treatment was given each day it is likely that the true TDF was 8 to 12% greater. The other eight patients who sustained radiation myelitis were all treated with six fractions and opposing fields. Their cord doses ranged from 3373 to 3526 cGy. The cord TDF ranged from 83.7 to 88.8 (Table II).

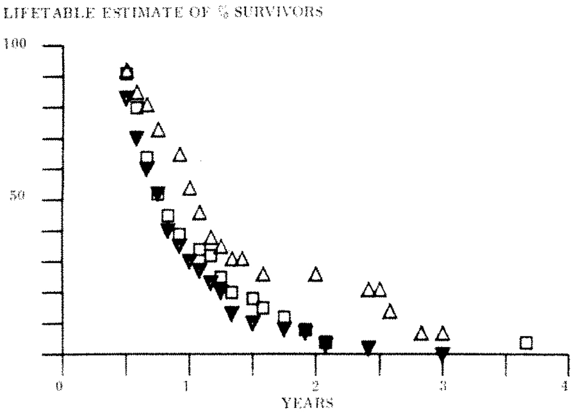


FIG. 1.

A lifetable relating survival to calculated radiation dose to spinal cord. For this table the patients have been divided into three groups: those receiving 3350 cGy or less (▼), 3351 to 3450 cGy (□) and greater than 3450 cGy (△). There is a significant trend relating survival and dose (P = 00.13).

If we examine the group of patients who received treatment entirely with opposing fields using a six-fraction technique, we find that all eight cases of radiation myelitis occurred in the 70 patients who received 3350 cGy or greater to the spinal cord. None occurred in the 60 patients who received a lower dose. One possible explanation for the absence of cord damage in those given less than 3350 cGy is the inclusion of cases with advanced disease or impaired general condition who may not have survived sufficiently long beyond six months to show radiation myelopathy. The lifetable method (Peto *et al.*, 1977) is particularly appropriate for analysis of this material. A lifetable of survival (Fig. 1) shows a trend towards improved survival with increasing dose levels. Figure 2 is a lifetable which estimates the probability of patients remaining free from radiation myelitis. In this analysis patients dying of tumour or co-existing disease fall out of the analysis at the end of their trial time "radiation myelitis

TABLE II

PATIENTS SUFFERING RADIATION MYELITIS

		Radiotherapy				Spinal cord dose				
				Dose						
Age	Sex	Fractions	Overall time (days)	cGy (rad)	TDF	cGy (rad)	TDF	Status	Survival (months)	Onset of radiation myelitis after radiotherapy (months)
47	M	20	29	4810*	86.3	4977	90.9	Dead	16	7
66	M	6	18	3498	89.4	3452	87.6	Alive	36	34
75	M	6	18	3420	86.3	3373	84.5	Dead	25	18
56	M	6	18	3420	86.3	3375	84.6	Alive	44	25
67	M	6	20	3600	91.7	3526	88.8	Dead	34	22
63	M	6	22	3498	86.4	3427	83.7	Dead	18	10
59	F	6	18	3498	89.4	3453	87.6	Dead	13	9
67	M	6	22	3498	86.4	3450	84.5	Dead	19	14
70	M	6	22	3498	86.4	3426	83.7	Dead	15	8

*Dose measured at mid-line, in remainder the maximum tissue dose is given.

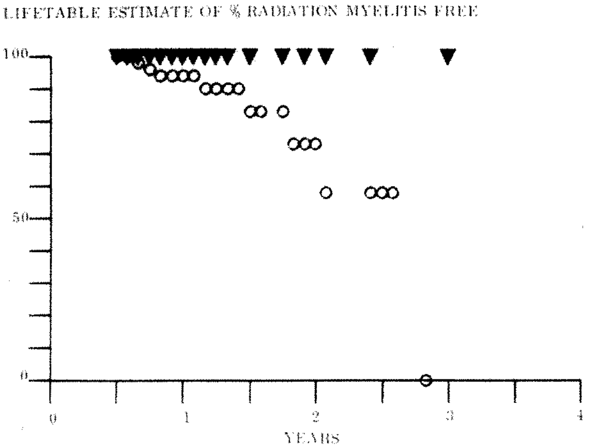


Fig. 2.

A lifetable relating freedom from radiation myelitis and calculated radiation dose to spinal cord. For this table patients have been divided into those receiving 3350 cGy or less (▼) and those who received a greater dose (○). Despite reduced survival in the lower dose group there is a significant relationship between dose and radiation myelitis ($P = 0.015$).

TABLE III

A comparison of the patients who developed radiation myelitis with those who did not, after treatment with six fractions to a total spinal cord dose exceeding 3350 cGy

		Radiation myelopathy	
		Not observed	Observed
Sex	Males Females	51 11	7 1
Site of primary	Left Right	28 34	2 6
Histology	Squamous Oat Other Not known	26 6 14 16	3 1 3 1
Machine employed	8 MV linear accelerator Cobalt	60 2	8 0
Sensitizer employed	Yes No	3 59	1 7
Age (years)	Mean SD	64.4 7.5	65.1 6.0
Systolic BP (mm Hg)	Mean† SD	147.5 20.5	155.7 26.4
Diastolic BP (mm Hg)	Mean† SD	87.9 12.2	91.4 12.15
Hb (g)	Mean‡ SD	13.2 1.9	14.8* 1.1
Length of field (cm)	Mean SD	15.3 2.0	15.3 3.2
Area of field (cm^2)	Mean SD	180.1 36.2	182.5 49.3
A–P distance (cm)	Mean SD	20.5 2.0	20.4 1.9
Cord dose (cGy)	Mean SD	3425 47.7	3435 48.5
Cord dose (TDF)	Mean SD	85.8 2.4	85.6 2.0

*Mean significantly different ($P = 0.05$)
†Cases available—24 and 7
‡Cases available—42 and 7

free". Cord damage is significantly related to radiation dose ($P = 0.016$). The incidence of radiation myelitis rises with time and it would seem likely that had more of these patients survived, radiation myelitis would have occurred in most of those who received more than 3350 cGy. Both patients who have now survived over three years are suffering from radiation myelitis.

In looking for a relationship between incidence of myelitis and dose above 3350 cGy we found that there were two cases among the 19 receiving between 3351 and 3400 cGy, three in the 25 who received between 3401 and 3450 cGy and three in the 26 who had doses above 3450 cGy. Therefore these data show no evidence of a relationship between the dose and the incidence of radiation myelitis above the level of 3350 cGy.

We have attempted to compare the incidence of myelopathy in those patients treated with the 20-fractions regime with those treated with six. There are only 18 patients who received more than 83 TDF to the spinal cord with opposing fields in 19–21 fractions. We cannot, therefore, make a meaningful comparison because of inadequate numbers, but it is of interest that the only case of radiation myelitis in this group was given a much higher dose to the spinal cord when expressed in TDF compared with those suffering myelopathy after treatment in six fractions.

Having defined the patients who received more than 3350 cGy to the spinal cord in six fractions over 18 days (83 TDF) who are at risk of radiation myelopathy, we can compare those who have developed radiation myelitis with those who have not, to see if there are precipitating factors. In Table III 62 patients without myelopathy are compared with the eight who suffered it. There was only one female among those with myelitis compared with seven males, but this is in keeping with the overall ratio.

Six of the patients with myelopathy showed tumours of the right lung as compared with only two on the left. Tumours on the right side generally dominate and it is difficult to imagine that this distribution is of any significance.

All eight patients with myelopathy were treated with the 8 MV machine and only two in this dose range, without myelopathy, were treated on a cobalt unit. The remaining patients treated with cobalt had cord doses below 3350 cGy. This is partly related to the policy adopted about dose during the period when cobalt units were used for these patients and partly to the greater fall in dose from the maximum beneath the skin to the depth of the spinal cord when dose distributions with a cobalt unit are compared with those of the 8 MV linear accelerator.

The haemoglobin concentration, however, was significantly higher in the myelopathy patients than in the others. A lifetable analysis on this group of patients showed that the level of haemoglobin, provided it was in the normal range, was not related to survival. We cannot, therefore, explain the findings by a longer period at risk of developing myelopathy in those with a high haemoglobin level.

The only significant difference in the parameters observed in those who suffered and those who did not suffer radiation myelopathy is in the haemoglobin levels at the time of treatment.

DISCUSSION

The extensive literature concerned with radiation myelopathy has been reviewed by Pallis *et al.*, (1961); Dynes and Smedal (1960); and Wara *et al.*, (1975). This series differs from all previous ones in the relative uniformity of the case material. All patients were under the care of the same consultant, all suffered locally-advanced carcinoma of bronchus and those in the definitive group were treated twice weekly to a total of six fractions.

There has been much discussion as to the total incidence of radiation myelopathy among patients treated by radiotherapy for malignant tumours where the cord is included in the field of treatment. A total incidence of nine cases in a series of 277 seems low compared with other figures recorded. The composition of the case material with particular regard to cord dosage, the duration of survival and the quality of the follow-up data greatly influence the incidence observed in any series. It must be acknowledged that with such a lethal tumour as carcinoma of bronchus where the final illness may assume many different patterns due to metastatic disease as well as to growth in the chest, radiation myelopathy may not receive recognition. Further, the bulk of the patients may not survive long enough to show this complication. The lifetable method is therefore of particular value in attempting to assess the relationship between incidence of radiation myelopathy and time. It would seem that in those treated with six fractions to a cord dose of greater than 3350 cGy (83 TDF) (Fig. 2) there is a steeply rising incidence; if many patients treated in this way had survived long-term, radiation myelitis might have occurred in the majority.

Radiation myelitis has not been observed in any patient given less than 3350 cGy (83 TDF) to the cord in six fractions. Above this level the incidence did not appear to rise with increasing dose; however, with only a limited number of patients showing myelopathy we must be cautious in interpretation.

There is a suggestion from these data that there may be a greater risk of radiation myelopathy in patients given six fractions compared with those given 20, when comparable radiation doses using the TDF formula are employed. A relative increase in late damage with limited fractionation would be in keeping with observations made by Bates and Peters (1975) upon the late effects following irradiation to the breast and with those of Bennett (1978) following radiotherapy for carcinoma of the cervix, as well as with those of Withers *et al.* (1978) in work with pig skin.

The relationship between haemoglobin level at the time of treatment and the incidence of radiation myelopathy is an interesting one. There seems no relationship between haemoglobin levels in these patients and survival. It may be, therefore, that at the lower levels which are regarded as adequate for radiotherapy there is a lowered oxygen tension in the spinal cord, thus leading to some degree of radioprotection. This would be the corollary of the increased radiosensitization observed when patients are treated in hyperbaric oxygen. A further investigation of the relationship between haemoglobin level and radiation damage in various normal tissues would seem justified.

The relationship seen in Fig. 1 between radiation dose to the cord and survival was unexpected. Among those patients treated in the lower two strata were some where the dose was reduced because of extensive disease or poor general condition. Those in the two remaining strata were selected on the same criteria and are entirely comparable. One must be cautious in interpretation of the data derived from a retrospective analysis of patients treated in consecutive fashion, but the policy of management was consistent through this period and we can conclude that in our patients who survived at least six months there was a suggestion that radiation dose and further survival are directly related. Local tumour control in a recent series of 50 cases treated by radiotherapy has been shown to be important in determining the survival in carcinoma of bronchus (Saunders *et al.*, 1980) and so radiation dose may well be significant in prolonging life. It follows that the dose which will give the best survival in the absence of cord shielding is that which will cause a high incidence of radiation myelitis. To achieve better results in carcinoma of bronchus, techniques of radiotherapy must be employed where higher doses can be given to the tumour and the spinal cord spared (Saunders *et al.*, 1980). Of the 38 patients who were excluded because a plan was employed to avoid radiation of the cord, none showed radiation myelitis.

For the time being, when using the six fraction treatment, we set a limit of 3250 cGy cord dose. Using opposing fields we achieve this by planning all treatment with the patient prone. The posterior field on the last of the six treatments is modified with a lead shield over the spinal cord. This, theoretically, achieves the reduction of dose required but the practical aspects of this method are undergoing analysis and a study of alternative techniques is being pursued. So far no patient has shown radiation myelopathy. Some reduction of dose in the "tumour volume" must occur, but this reduction would be less than that in the spinal cord because of its more anterior position.

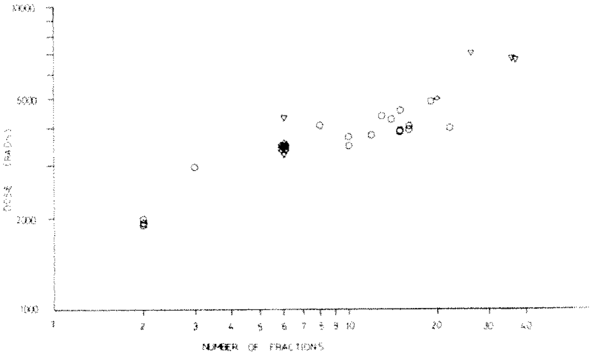


FIG. 3.

A scatter diagram relating radiation dose and fractionation in patients presenting radiation myelitis after treatment to the thoracic cord. Shown are the cases recorded in this paper (◇), those observed by Wara *et al.* 1975 at the University of California Medical Centre San Francisco (▽) and other cases found in the literature of the same authors (○).

This study makes it possible to fix with some accuracy the level of dose at which radiation myelopathy occurs when giving radiotherapy in six fractions. A cord dose of 3350 cGy agrees well with the dose fractionation plot for radiation myelitis presented by Wara *et al.* (1975) (Fig. 3). We would agree with their suggestion that a central registry for all cases of nervous tissue damage should be established so as to determine most accurately the safe levels for irradiation of the spinal cord.

ACKNOWLEDGMENTS

We wish to thank Dr. Michele Saunders who undertook much of the clinical care of the patients and our colleagues in chest medicine who continued their close co-operation, also Mrs. Gail Fuller of the Cancer Registry at Mount Vernon and Mrs. Eileen Davies who prepared the manuscript. The support of the Medical Research Council is gratefully acknowledged.

REFERENCES

AHLBOM, H. E., 1948. The results of radiotherapy of hypopharyngeal cancer at the Radiumhemmet, Stockholm, 1930–1939. *Acta Radiologica, 22,* 155–171.

ASSCHER, A. W. and ANSON, S. G., 1962. Arterial hypertension and irradiation damage to the nervous system. *Lancet, ii,* 1343–1346.

BATES, T. D. and PETERS, L. J., 1975. Danger of the clinical use of the NSD formula for small fraction numbers. *British Journal of Radiology, 48,* 773.

BENNETT, M. B., 1978. The treatment of stage III squamous carcinoma of the cervix in air and hyperbaric oxygen. *British Journal of Radiology, 51,* 68.

BODEN, G., 1948. Radiation myelitis of the cervical spinal cord. *British Journal of Radiology, 21,* 464–469.

BRENK, H. A. S. VAN DEN, RICHTER, W. and HURLEY, R. H., 1968. Radiosensitivity of the human oxygenated cervical spinal cord based on analysis of 357 cases receiving 4 MeV X-rays in hyperbaric oxygen. *British Journal of Radiology, 41,* 205–214.

BRINKLEY, D. and MASTERS, H. E., 1967. The depth of the spinal cord below the skin. *British Journal of Radiology, 40,* 66–68.

CADE, I. S., and MCEWEN, J. B., 1978. Clinical trials of radiotherapy in hyperbaric oxygen at Portsmouth (1964–1976). *Clinical Radiology, 29,* 333–338.

CHURCHILL-DAVIDSON, I., FOSTER, C. A., WIERNIK, G., COLLINS, C. D., PIZEY, N. C. D., SKEGGS, D. B. L. and PURSER, P. R., 1966. The place of oxygen in radiotherapy. *British Journal of Radiology, 39,* 321–331.

COY, P. and DOLMAN, C. L., 1971. Radiation myelopathy in relation to oxygen level. *British Journal of Radiology, 44,* 705–707.

DYNES, J. B. and SMEDAL, M. L., 1960. Radiation myelitis. *American Journal of Roentgenology, 83,* 78–87.

JONES, A., 1964. Transient radiation myelopathy (with reference to Lhermitte's sign of electrical paraesthesia). *British Journal of Radiology, 37,* 727–744.

PALLIS, C. A., LOUIS, S. and MORGAN, R. L., 1961. Radiation myelopathy. *Brain, 84,* 460–479.

PETO, R., PIKE, M. C., ARMITAGE, P., BRESLOW, N. E., COX, D. R., HOWARD, S. V., MANTEL, N., MCPHERSON, K., PETO, J. and SMITH, P. G., 1977. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. *British Journal of Cancer, 35,* 1–39.

SAUNDERS, M. L., DISCHE, S., MARTIN, W. M. C., ANDERSON, P. and LEE, M. E., 1981. A controlled clinical trial of misonidazole in carcinoma of the bronchus. (In preparation.)

SMITHERS, D. W., CLARKSON, J. R. and STRONG, J. A., 1943. The roentgen treatment of cancer of the esophagus. *American Journal of Roentgenology*, *49*, 606–634.

STEVENSON, L. D. and ECKHARDT, R. E., 1945. Myelomalacia of the cervical portion of the spinal cord, probably the result of roentgen therapy. *Archives of Pathology*, *39*, 109–112.

WARA, W. M., PHILLIPS, T. L., SHELINE, G. E. and SCHWADE, J. G., 1975. Radiation tolerance of the spinal cord. *Cancer*, *35*, 1558–1562.

WITHERS, H. R., THAMES, H. D., FLOW, B. L., MASON, K. A. and HUSSEY, D. H., 1978. The relationship of acute to late skin injury in 2 and 5 fraction/week γ-ray therapy. *International Journal of Radiation, Oncology, Biology, and Physics*, *4*, 595–601.

Book reviews

Therapy and Prevention of Infections in Cancer Patients. Edited by M. Glauser and J. Klastersky, pp. vii+80, 1979 (European Journal of Cancer Supplement) (Pergamon Press: Oxford), $21.00.
ISBN 0-08-024434-3

This volume, a supplement to the European Journal of Cancer, comprises the papers presented at a symposium of the European Organisation for Research and Treatment of Cancer (EORTC), held at Lausanne in 1978. Many of the presentations represent "work in progress" and this publication is a useful and quite up-to-date review of the subject. It is divided into two parts: Therapeutic Approaches to the Management of infection in Cancer Patients, and Immunoprophylaxis of Infection in Cancer Patients.

The first part includes judicious reviews by J. Klastersky of antibiotic combinations for severe infections and of the use of granulocyte transfusions, and by M. Dietrich of reverse isolation and gut decontamination, together with some experimental studies comparing antimicrobial agents in particular treatment centres. The predominant impression is of many questions that need to be answered before optimal management can be achieved, and this is acknowledged by the contributors. The report by H. Gaya on the EORTC large-scale prospective controlled clinical trial of empirical antimicrobial treatment and of the initial results of an extension of this to refine choice of antimicrobial and to assess the role of granulocyte transfusion, is therefore particularly welcome. In the first trial, combinations of any two of the three agents, gentamicin, cephalothin and carbenicillin, were compared. In brief, the results confirmed that early well-chosen empirical therapy could improve the prognosis and that response was particularly dependent on the level of circulating granulocytes, and showed gentamicin and carbenicillin to be the most effective combination in some types of patient and of infection. The combination of cephalothin and gentamicin often produced renal problems, but the use of cefazolin with an aminoglycoside (amikacin) in the second trial did not have this effect.

The second part of the symposium, by A. I. Braude and others, describes experimental work on a different approach, the production of immunity to the core-glycolipid of endotoxin, which luckily is very similar across the range of gram-negative bacilli that cause infection in neutropenic patients. Laboratory experiments and an early clinical trial with promising results are presented, and it appears that this mechanism may well become an important element in prophylaxis and management, complementing the antimicrobials, granulocyte transfusions and protective measures discussed earlier.

D. C. E. SPELLER.

Cancer and the Immune Response. By G. A. Currie. 2nd ed., pp. 129, 1980 (Edward Arnold, London), £9·75.
ISBN 0-7131-4356-8

This is a second edition of a previously very successful book that has been accepted as providing an overview of the subject of immunology of cancer. So fast has the subject matured that a revision is highly welcomed. This book is a genuine update in both detail and in presentation.

Getting a subject into perspective is a problem with any topic, but particularly so with cancer and immunology. The first, cancer, is a major force in our society to motivate research and its support: the second, immunology, is a science of its own with a proven track record in clinical management of bacterial and viral disease. The combined subject is like a minefield to the incautious, particularly when hypotheses derived from tissue-culture or animal-model studies are examined in the light of clinical experience of human disease. A guide to the minefield is immensely valuable, and this is what the book sets out to be. Designed for the clinician, a reader's basic knowledge of haematology, biochemistry and immunology is assumed, as is a familiarity with oncology.

Evidence for tumour-specific antigens in experimental animals is presented before setting out the hypotheses for immunological mechanisms that might be operative in cancer. This is followed by several chapters of evidence for and against the hypotheses. From these beginnings the author builds up a picture of the evidence for immune surveillance and antigenicity of tumours and then argues the possibilities for immunotherapy and immunodiagnosis. A balanced view is maintained throughout by the ploy of viewing a topic first from one side, building up the arguments, and then from a totally different side. It is thus necessary to read any section as a whole. It is not possible to take any paragraph out of context. Nevertheless the supporting literature has been thoroughly researched for the key works on each subject and this second edition has updated and extended the survey of the first.

The style is coherent and very readable, the content is comprehensive. Because of the range of the content, the book is to be recommended as essential reading for both clinicians and scientists with an involvement in oncology.

A. W. PREECE.

1981, *British Journal of Radiology*, *54*, 36–39

The relationship of dose to prognosis in squamous-cell carcinoma of the aerodigestive tract

By M. Wollin, M.S. and A. R. Kagan, M.D.

Southern California Permanente Medical Group, Department of Radiation Therapy, 1510 North Edgemont, Los Angeles, California 90027, USA

(*Received March 1979 and in revised form June 1980*)

ABSTRACT

How much does radiation dose determine prognosis of patients requiring radiotherapy for squamous-cell carcinoma of the aerodigestive tract? Using a statistical test of the correlation of dose versus outcome, several results of radiation treatment reported in the literature were examined. The radiation dose received was found to be a poor predictor of which patients would be cured.

The Ellis (1969) formula for nominal standard dose (NSD) has been used to evaluate the tolerance of normal tissue. Liversage (1971), Orton and Ellis (1973), Cohen (1966), Fowler (1971), Lajtha and Oliver (1961), and Umegaki *et al.* (1974) have all suggested modifications of the basic structure of the Ellis formula. Wollin and Kagan (1976) have suggested that major changes are needed to allow for the extreme variations in amount of daily dose and fractionation. Certainly, isoeffect formulas are needed that can satisfactorily equate one dose–time regime with another. However, equally and perhaps even more important is the question of the extent to which the dose delivered determines the outcome. To what degree does the amount of radiation determine cure or failure, injury or non-injury? Friedman and Brucer (1959) once indicated that tumour cure depended on biology (60%), clinical judgement (30%), and technique (10%). Recent knowledge about tumour size, staging, the cell cycle, labelling index, and exponential and plateau tumour growth have somewhat illuminated the dark void of biology. Clinical judgement has been enriched by physicians working together in multidisciplinary specialized cancer clinics. Techniques have improved with increased awareness of the capabilities of different high-energy machines and attention to technical errors that occur.

We examine here the hypothesis that dose is the main determinant in effecting cure or failure in the treatment of squamous-cell tumours of the aerodigestive tract.

METHODS AND MATERIALS

The extent to which radiation dose determines outcome can be estimated by calculating the point biserial correlation coefficient (RPB) (Bahn, 1972). Ideally, the higher the dose the greater the biological effect and therefore the larger the correlation between dose and effect. The test does not require grouping of data into various dose levels but is calculated point by point. A perfect correlation would give an RPB of +1, and an RPB of 0 shows no correlation. We used Student's t test to determine the level of significance in order to rule out chance correlation because of small sample size.

If the RPB is squared and multiplied by 100, the resulting value is called the coefficient of determination (RPB^2) (Bruning and Klintz, 1968). The RPB^2 can be thought of as giving a percentage estimate of how dose changes the clinical outcome: the number of complications and morbidity, or cures and failures, depends on dose. An RPB^2 of 30% indicates that at least 30% of the variability of the clinical outcome must be explained by dose, time, and fractionation. If dose and technique are the major factors determining outcome, then the RPB^2 approaches 100%. An RPB^2 of 10%, however, means that 90% of the variability of the outcome is determined by factors other than dose, such as biological factors inherent in the tumour of the host.

An example of the use of RPB^2 is demonstrated by Fig. 1. For curve A, the RPB is positive, the p value is significant, and the high RPB^2 value indicates that dose in this instance plays a large part in determining outcome. For curve B, the steadily increasing cure rate with increased dose is confirmed by the relatively high values of RPB and RPB^2. In curve C, the RPB is negative, the p value is low and the low RPB^2 indicates that dose is a minor factor in determining outcome.

The RPB^2 was used to examine various radiation treatment schedules reported in the literature for the aerodigestive tract, in order to analyse correlations between dose and outcome. These data were also analysed using a linear logistic model (Cox, 1970) as

---

Reprint requests to: Myron Wollin, M.S., Southern California Permanente Medical Group, Department of Radiation Therapy, 1510 North Edgemont, Los Angeles, California 90027.

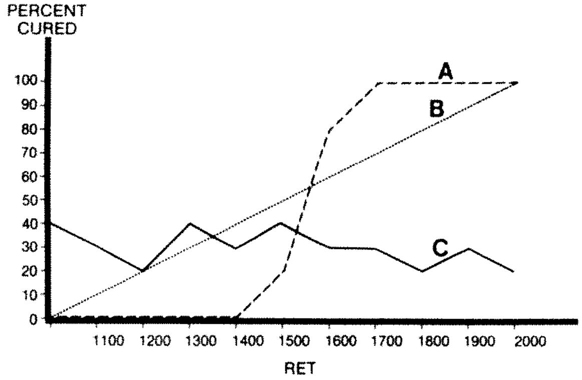


FIG. 1.

Three possible dose–response surves. The point biserial correlation (RBP) expresses the extent to which dose determines outcome

	RPB	RPB^2	p
Curve A	+0.854	73.0%	< 0.0005
Curve B	+0.632	40.0%	< 0.0005
Curve C	−0.075	0.6%	Not significant

a check on the RPB^2 methodology for two sites where stage of disease and dose could be determined.

RESULTS

The series analysed from the literature are listed in Table I. Fletcher and Klein (1964) treated 40 patients for supraglottic tumours, 25 of which were cured. Six with laryngeal oedema were excluded. The total dose was 5000 to 7400 cGy (rad) at a daily dose of 150 to 316 cGy (rad). Dose defined by NSD showed no capacity to predict which patients would be cured.

Ghossein *et al.* (1974) treated squamous-cell carcinoma of the supraglottic larynx. Fifty-eight of 81 patients with T1 and T2 (early) lesions and 59 of 122 patients with T3 or T4 (late) lesions did not have a recurrence after two years. The total dose was 3650 to 9700 cGy (rad) at a daily dose of 154 to 287 cGy (rad). The dose described by NSD did not predict cure of early or late lesions.

Friedman (1974) treated 117 patients for squamous-cell carcinoma of the upper air passages, 66 of whom were cured for five years after treatment. The total dose was 4500 to 11 000 cGy (rad) at a daily dose of 132 to 450 cGy (rad). The NSD did not predict which patients would be cured.

Fayos (1975) treated 192 patients who had squamous-cell carcinoma of the endolarynx, eight of whom were excluded because their outcome was undetermined. One hundred and twenty-nine patients did not suffer recurrence for five years after treatment. The total dose was 6000 to 7170 cGy (rad) at a daily dose of 143 to 224 cGy (rad). NSD did not predict which patients would be cured.

In the Shukovsky and Fletcher (1973) series of squamous-cell carcinoma of the tonsillar fossa, 35 of 40 patients with T1 and T2 lesions and 28 of 42 patients with T3 or T4 lesions had primary control after three years as shown on their time–dose scattergrams. The total dose was 5300 to 7500 cGy (rad) at a daily dose of 167 to 328 cGy (rad). The NSD did not predict which patients would be cured of T1 or T2 lesions. The NSD did, however, show some capacity to predict which patients would be cured of T3 or T4 lesions. When the data for all stages were combined, NSD again did not show any capacity to predict outcome.

Andrews (1965) treated 43 patients for squamous-cell carcinoma of the aerodigestive tract, 12 of whom were alive three years after treatment. The total dose was 7080 to 10000 cGy (rad) at a daily dose of 98 to 270 cGy (rad). The NSD did not show any ability to predict which patients will be alive three years after treatment.

Moench and Phillips (1972) treated squamous carcinoma of the nasopharynx. Forty-two of 54 selected patients with T1 lesions were locally controlled for three years. The total dose was 2700 to 6700 cGy (rad) at a daily dose of 120 to 290 cGy (rad). The NSD did show some ability to predict local control after three years.

Shukovsky (1970) treated 114 patients with squamous-cell carcinoma of the supraglottic larynx T1–T4, 79 of which were controlled. The total dose was 4900 to 7800 cGy (rad) at a daily dose of 150 to 315 cGy (rad). The NSD did not show any ability to predict which patients were controlled.

When all the data on cure of aerodigestive carcinoma were combined, NSD still did not show any capacity to predict which patients would be cured.

Using a linear logistic model with a binary response variable, the data of Shukovsky and Fletcher (1973) and of Ghossein *et al.* (1974) were re-analysed. When these data were evaluated for stage, dose and outcome, neither the dose expressed by NSD nor the physical dose gave good prediction of outcome.

DISCUSSION

There are two studies that show a significant correlation of dose with outcome at the 0.05 level with the RPB analysis—Shukovsky and Fletcher (1973) for T3, T4 tonsillar fossa and Moench and Phillips (1972) for T1 nasopharynx. No other studies showed significance at that level. These two studies suggest that stage is important. However, when the data of Shukovsky and Fletcher (1973) were re-examined for each stage, using the linear logistic model, that is for T1, T2, T3 and T4 individually, dose did not give a good prediction of outcome. When all stages were combined the result was not significant. This could be explained on the basis of biological and dosimetric variations among the various stages or perhaps some bias in assigning patients to the various stages.

Interestingly, Shukovsky (1970) claims a correlation with dose for T2, T3 supraglottic larynx but the data available for analysis by us are for all stages combined and did not show a correlation. Ghossein *et al.* (1974), also for supraglottic larynx, did not show any correlation whether by individual stage or by combining all stages, though the cure rate doubled from 43% to 89% for Stages T1 and T2. Again, when Ghossein's data were reanalysed for stage using the linear logistic model, dose did not give a good prediction of outcome.

When the data for all centres were combined, no

TABLE I

Prognosis determined by dose in squamous cell carcinoma of the aerodigestive tract

Source of data	Irradiated area	NSD range (ret)	Patients cured/total	Percent patients cured	RPB	RPB^2 (%)	Significance at 0.05 level
Fletcher and Klein (1964)	Supraglottic larynx	1500–1900 1900–2200	10/14 15/20	71 75	+0.060	0.4	NS
Ghossein *et al.*, (1974)	Supraglottic larynx, T1, T2	1650–1950 1950–2250 2250–2650	6/14 36/49 16/18	43 73 89	+0.172	2.9	NS
	Supraglottic larynx, T3, T4	1150–1950 1950–2250 2250–2650	13/25 29/62 17/35	52 47 49	−0.031	0.1	NS
	Supraglottic larynx, all stages	1200–2150 2150–2700	56/96 61/107	58 57	+0.350	0.1	NS
Friedman (1974)	Aerodigestive tract	1400–2450 2540–3300	31/58 35/59	53 59	+0.061	0.4	NS
Fayos (1975)	Endolarynx	1600–1850 1850–2100	55/70 74/114	79 65	−0.112	1.2	NS
Shukovsky and Fletcher (1973)	Tonsillar fossa, T1, T2	1700–1900 1900–2200	21/24 14/16	88 88	+0.004	0	NS
	Tonsillar fossa, T3, T4	1600–1800 1800–2000 2000–2200	2/5 12/23 14/14	40 52 100	+0.285	8.1	$p < 0.05$
	Tonsillar fossa, all stages	1600–1900 1900–2200	30/39 33/43	77 77	+0.120	1.4	NS
Andrews (1965)	Aerodigestive tract	1700–2200 2200–2500	4/25* 8/18*	16 44	+0.163	2.7	NS
Moench and Phillips (1972)	Nasopharynx T1	1000–1500 1500–1700 1700–2200	17/24 12/15 13/15	71 80 86	+0.230	5.3	< 0.05
Shukovsky (1970)	Supraglottic larynx, all stages	1500–1900 1900–2300	38/57 41/57	67 72	+0.039	0.2	NS
Combined data from literature	Aerodigestive	1200–1900 1900–3300	261/382 272/449	68 61	−0.80	0.6	NS

*Alive after three years.

significance was found. By combining centres one confounds the problems of consistent dosimetry, patient care, staging, etc. which could help to explain the results. But it is also possible that with more data available by combining centres, significance might be found where it did not appear when only small numbers are available from each centre. This was demonstrated recently with the hyperbaric experience of the Medical Research Council's Working Party (Windeyer, 1978) where each individual centre did not show significance but a significant result was found when all the centres were combined.

NSD was used to determine the relative biological effect of the different treatment schedules examined. The exponents of the isoeffect formulae can be changed, but the clinical data must be subjected to an analysis such as the G (Kagan *et al.*, 1973) or RPB in order to ensure that the difference between cure and failure is caused by variation of dose and not by other factors such as selection of patients.

Most isoeffect lines are drawn by the least-squares method of calculation or by visually estimating the average slope. Few authors have concerned themselves with the problem of biological factors other than dose. Most investigators have devoted their efforts to different mathematical expressions of dose rather than to addressing the problem of defining the role of dose in determining outcome. Each isoeffect point that is used to determine the isoeffect line has an uncertainty associated with it; to ignore this uncertainty makes analysis of clinical data misleading.

Radiation therapy presumably does cure carcinoma of the aerodigestive tract. If zero dose were given and compared with the doses normally employed in radiation therapy, surely correlation of outcome with dose would be found. But over the limited range of doses employed in therapy, the biology, clinical care of the patient, etc. rather than the physical dose is the important parameter in determining outcome.

CONCLUSION

Many investigators assume that dose determines cure and failure in the treatment of tumours of the aerodigestive tract. Our analysis of dose and dose-related-to-stage indicates that dose alone over the limited range of doses employed in radiation therapy is not significantly associated with cure or failure when six of eight clinical studies are analysed.

ACKNOWLEDGMENT

The authors thank Alan Forsyth, Ph.D., for statistical analysis of the data.

REFERENCES

ANDREWS, J. R., 1965. Dose-time relationships in cancer radiotherapy: a clinical radiobiology study of extremes of dose and time. *American Journal of Roentgenology, 93,* 56–74.

BAHN, A. K., 1972. Highlights of miscellaneous topics. In *Basic Medical Statistics,* (Grune and Stratton, New York) pp. 174–200.

BRUNING, J. L. and KLINTZ, B. L., 1968. *Computational Handbook of Statistics,* (Scott, Foresman & Co., Glenview, Illinois) pp. 163–166.

COHEN, L., 1966. Radiation response and recovery: radio biological principles and their relation to clinical practice. In *The Biological Basis of Radiation Therapy,* ed. E. E. Schwartz (J. P. Lippincott, Philadelphia) pp. 208–348.

COX, D. R., 1970. *Analysis of Binary Data* (Methuen, London).

ELLIS, F., 1969. Dose, time and fractionation: a clinical hypothesis. *Clinical Radiology, 20,* 1–7.

FAYOS, J. V., 1975. Carcinoma of the endolarynx: results of irradiation. *Cancer, 35,* 1525–1532.

FLETCHER, G. H. and KLEIN, R., 1964. Dose-time-volume relationships in squamous cell carcinoma of the larynx. *Radiology, 82,* 1032–1042.

FOWLER, J. F., 1971. Experimental animal results relating to time-dose relationships in radiotherapy and the "ret" concept. *British Journal of Radiology, 44,* 81–90.

FRIEDMAN, M., 1974. Clinical studies of the complexities of the recovery and allied factors. In *Biological and Clinical Basis of Radiosensitivity,* ed. by M. Friedman (Charles C. Thomas, Springfield, Illinois), pp. 389–430.

FRIEDMAN, M. and BRUCER, M., 1959. Summary of the symposium. In *Roentgens, Rads and Riddles,* ed. by M. Friedman, M. Brucer, E. Anderson (U.S. Government Printing Office, Washington D.C.). p. x.

GHOSSEIN, N. A., BATAINI, J. P., ENNUYER, A., STACEY, P. and KRISHNASWAMY, V., 1974. Local control and site of failure in radically irradiated supraglottic laryngeal cancer. *Radiology, 112,* 187–192.

KAGAN, A. R., LEE, K. H., WOLLIN, M. and NORMAN, A., 1973. An examination of some dose-time relationships in therapeutic radiology. *British Journal of Radiology, 46,* 354–359.

LAJTHA, L. G. and OLIVER, R., 1961. Some radiobiological considerations in radiotherapy. *British Journal of Radiology, 34,* 252–257.

LIVERSAGE, W. E., 1971. A critical look at the ret. *British Journal of Radiology, 44,* 91–100.

MOENCH, H. C. and PHILLIPS, T. L., 1972. Carcinoma of the nasopharynx. *The American Journal of Surgery, 124,* 515–518.

ORTON, C. G. and ELLIS, F., 1973. A simplification in the use of the NSD concept in practical radiotherapy. *British Journal of Radiology, 46,* 529–537.

SHUKOVSKY, L. J., 1970. Dose, time, volume relationships in squamous cell carcinoma of the supraglottic larynx. *The American Journal of Roentgenology, 108,* 27–29.

SHUKOVSKY, L. J. and FLETCHER, G. H., 1973. Time-dose and tumor volume relationships in the irradiation of squamous cell carcinoma of the tonsillar fossa. *Radiology, 107,* 621–626.

UMEGAKI, Y., URANO, M. and MAKANO, M., 1974. Optimum dose fractionation schemes in radiotherapy of human cancer. Part I: The role of fractionation radiotherapy. In *Fraction Size in Radiobiology and Radiotherapy,* ed. T. Sugahara, L. Revesz and O. C. A. Scott (Williams and Wilkins, Baltimore), pp. 188–189.

WINDEYER, SIR BRIAN, 1978. Hyperbaric oxygen and radiotherapy. *British Journal of Radiology, 51,* 875.

WOLLIN, M. and KAGAN, A. R., 1976. Modification of the biologic dose to normal tissue by daily fraction: model for calculating normal tissue tolerance. *Acta Radiologica (Therapy), 15,* 481–492.

1981, *British Journal of Radiology*, *54*, 40–47

Interaction of hyperthermia and radiation: radiation quality

By D. D. Loshek, Ph.D.*, J. S. Orr, D.Sc.† and E. Solomonidis, B.Sc.

Department of Clinical Physics and Bio-Engineering, West of Scotland Health Boards, Glasgow

(*Received March 1979 and in revised form May 1980*)

ABSTRACT

Cell-survival data were collected to determine the survival response of asynchronous CHO cells subject to radiation and hyperthermia. The irradiation was at room temperature 100 minutes before exposure to hyperthermia at 42°C. The survival response to the combination of these two agents is expressed by means of a survival surface, a three-dimensional concept relating cell survival to heat dose and radiation dose. The survival surface could be approximately described by a survival model comprising three components of cell killing: the unperturbed radiation component, the unperturbed hyperthermia component, and the interaction component. The dependence of the radiation component and the interaction component on radiation quality were investigated by irradiating with either ^{60}Co γ rays, 250 kV X rays or 14.7 MeV neutrons. An analysis suggests that the interaction component and the radiation component exhibit similar dependencies on radiation quality both for the deposition of damage and the repair or accumulation of that damage.

It has been known for some time that hyperthermia and radiation interact in their effects on cell survival (Belli and Bonte, 1963; Ben Hur *et al.*, 1972, 1974; Robinson and Wizenberg, 1974). More recently the effects of radiation quality on the interaction have been investigated (Hahn *et al.*, 1976; Gerner and Leith, 1977; Schrader-Reichhardt and Markus, 1978; Ngo *et al.*, 1978). However, the design of these experiments was such that very little information about the dependence on radiation quality of the interaction mechanism itself could be obtained.

In a previous paper (Loshek *et al.*, 1977a) an experimental design and method of analysis were presented that would allow a more detailed analysis of the interaction phenomenon. The combined effect of radiation and hyperthermia may be separated into three components of cell damage. The first is the cell damage that is due to the effects of radiation in the absence of heat. The second is the hyperthermia-induced damage unperturbed by the effects of radiation. The third component is the additional damage due to interaction that is responsible for the synergism between heat and radiation. It was demonstrated that this third component was approximately a linear function of both radiation dose and hyperthermia exposure. A survival model was presented (Loshek *et al.*, 1978) which suggested that the interaction was the result of the combined effects of two types of damage event specific to interaction; one deposited by radiation and one deposited by hyperthermia. An investigation of the temperature dependency of the hyperthermia-induced interaction damage (Loshek *et al.*, 1977b) revealed that this type of damage was significantly less temperature-sensitive than the unperturbed hyperthermia component of damage.

The present series of experiments deals with the effect of radiation quality on the properties of radiation-induced interaction damage. The effects of radiation doses probed by the subsequent hyperthermia exposure are analysed to explore the mechanisms of the deposition and repair or accumulation of interaction damage.

MATERIALS AND METHODS

Cell line

Chinese hamster ovary CHO cells were maintained in exponential growth in Hams F12 supplemented with 15% calf serum, non-essential amino acids, and 2 mM glutamine. The pH of the medium was maintained at 7.2 with 20 mM Hepes buffer. Asynchronous cells were harvested by trypsinization and treated in suspension.

Irradiation conditions

X rays were provided by a Siemens Stabilipan X-ray unit operating at 250 kV, 15 mA, and filtered to a half value thickness of 1.8 mm of copper. The focal distance was 30 cm where the dose rate was 1.35 Gy/min.

^{60}Co γ rays were provided by a teletherapy unit. The distance from the source was 46 cm where the dose rate was 0.96 Gy/min. Five mm of Perspex was placed between the source and the cell suspension to provide adequate build-up.

Neutrons of mean energy 14.7 MeV were produced by the D-T reaction in a sealed generator (type P, Marconi Elliott Avionic Systems Ltd.). A stack of six T30 flasks was placed at a distance of 8 to 17 cm corresponding to dose rates of 0.15 to 0.03 Gy/min. Gamma contamination of the beam was from 5±2 to 7±3% of the total dose, increasing over the distance from the bottom (nearest the

---

Present addresses: *Marshfield Clinic, Marshfield, Wisconsin, USA 54449; †Medical Physics Department, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS.

source) to the top of the stack. Uniformity of dose at the highest dose rate was 11% of the total dose. The relative and absolute dose rates were determined using tissue-equivalent ionization chambers.

X-ray and γ-ray doses were calculated as doses to muscle using the factors from ICRU Handbook 85. Neutron doses were calculated as doses to wet tissue using spectrum-weighted kerma values (ICRU 13, 1969), *W* values (Dennis, 1971) and stopping-power ratios, assuming that the stopping powers for solid and gaseous hydrocarbons are the same.

Heating techniques

Cells were heated in plastic T30 flasks which were held by the screw caps in groups of five or ten in a light Perspex rack constructed to accommodate 150 flasks. This rack allowed all the flasks to be submerged simultaneously and then removed in groups of five to ten at a time. The temperature in the flasks heated in this way rose exponentially with a half-time of 30 seconds. To minimize the initial depression of the water-bath temperature, the rack and complement of flasks were first heated for 15 minutes in another water-bath maintained at 37°C. At a temperature of 42°C, the rack and 120 flasks transferred from 37°C lowered the temperature by 0.3°C. The water-bath temperature typically recovered in five to eight minutes.

Grant SX-35 water-baths provided temperature stability of ±0.01°C. Thermometry was performed using precision mercury-in-glass thermometers, graduated at 0.05°C intervals. These were compared with a temperature standard calibrated by the National Physical Laboratory.

Experimental procedure

The cells were suspended at a concentration of 1.25×10^5 cells/ml in seven or five (for neutrons) plastic T30 flasks. Allowing one flask for a radiation control, the remaining flasks were irradiated in suspension with graded doses of X rays, γ rays, or neutrons at room temperature. The X and γ irradiations were sequential, the high-dose flasks being irradiated first and the low-dose flask last. The six irradiations required a time interval of 15 minutes. The neutron irradiations were performed simultaneously over a time interval of 25 minutes. The time interval required for additional cell manipulations, from the last irradiation to the start of heating, was standardized at 100 minutes. Unpublished studies of the decrease of interaction revealed that during the 100-minute interval very little relaxation occurred and that the change of interaction was very slow over the time interval required for the irradiations. This apparent disagreement with other published data (Henle and Leeper, 1976) may be due to the cells being maintained both at room temperature and in suspension during this period.

Each of the resulting seven or five populations was further diluted and distributed among a number of replicate T30 flasks at a concentration to yield 500 clones/flask if they were not further treated. One hundred minutes after the cells had been irradiated, heat treatment was started by immersing the flasks containing the suspended cells, except for controls from each population, in a water-bath maintained at a nominal temperature of 42°C. Multiple samples from each of the populations were removed at 15 minute intervals.

Four flasks were allotted for each survival point for cells that were not heated, three flasks for the heated but not irradiated survival points and two flasks for each heated and irradiated survival point. Since increasing numbers of cells were plated only for increasing radiation doses, but not for increasing hyperthermia doses, the number of clones per flask decreased for increasing hyperthermia dose. The parameters of both the survival surface and the individual curves were obtained by using a least χ^2 fit for the expected and observed numbers of clones per point. This technique takes account of the increasing variance associated with the decreasing numbers of clones per point.

The experimental procedure described above yields a hyperthermia survival curve for each radiation dose and a radiation survival curve for each hyperthermia dose. The above matrix experiment was performed three times for each radiation quality.

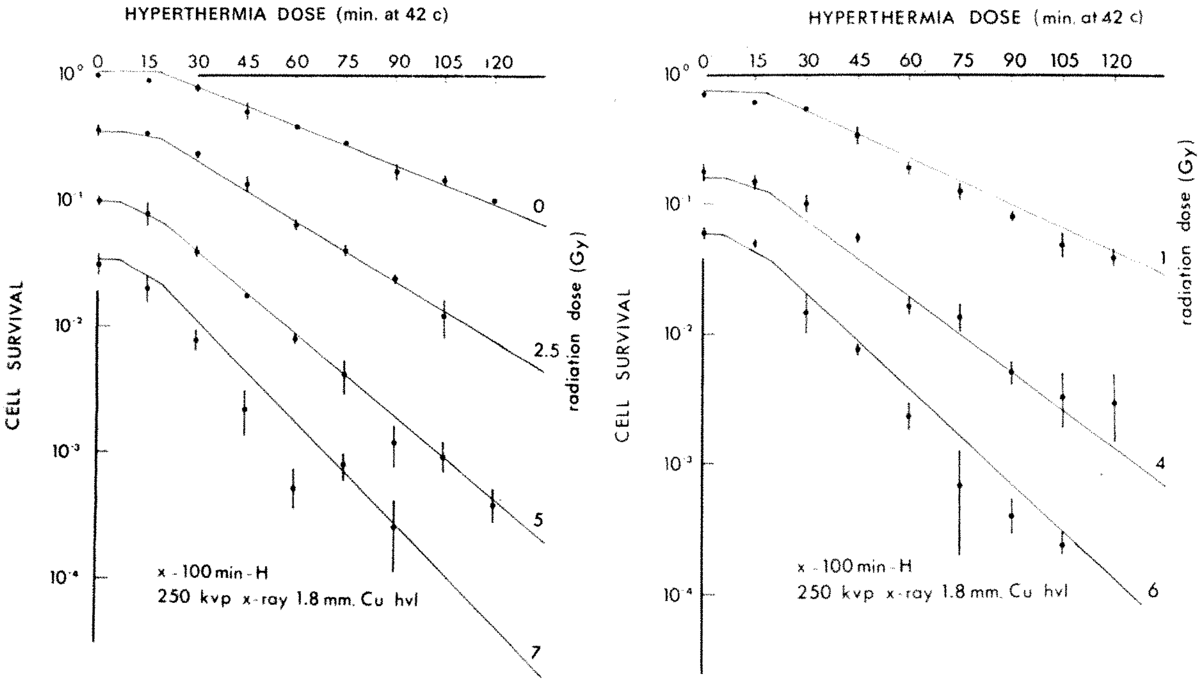
RESULTS

The data for three separate experiments for each type of radiation were pooled and used to determine the parameters of the survival equation, equation (1) (Loshek *et al.*, 1977a).

$$\ln S = D_1 K_R + t_1 K_H + D_2 t_2 K_I \qquad (1)$$

$$\begin{aligned} \text{where } D_1 &= D - D_q \text{ for } D > D_q \\ &= 0 \text{ for } D < D_q \\ D_2 &= D - D_q I \text{ for } D > D_q I \\ &= 0 \text{ for } D < D_q I \\ t_1 &= t - t_q \text{ for } t > t_q \\ &= 0 \text{ for } t < t_q \\ \text{and } t_2 &= t - t_q I \text{ for } t > t_q I \\ &= 0 \text{ for } t < t_q I \end{aligned}$$

and where: K_R = unperturbed radiation sensitivity
D_q = unperturbed quasi-threshold radiation dose
K_H = unperturbed thermal sensitivity



L FIG. 1. R

CHO cell survival as a function of hyperthermia dose 100 minutes after irradiation with 250 kV X rays. Data points represent the mean and standard error for three observations.

TABLE I

INTERACTION PARAMETERS (EQUATION 1) RADIATION—100 MIN—H

Parameter	Unit	Multiplying factor	^{60}Co γ	250 kV X	14.7 MeV n
K_R	Gy^{-1}	10^{-1}	5.15	5.01	8.95
K_H	min^{-1}	10^{-2}	2.04	2.46	2.68
K_I	Gy^{-1}min^{-1}	10^{-3}	4.77	5.48	7.69
D_q	Gy	10^{-1}	5.42	3.09	−0.13
t_q	min	10^{+1}	2.25	2.00	2.52
D_qI	Gy	10^{-1}	4.66	4.03	1.36
t_qI	min	10^{+1}	1.44	0.54	1.18
K_I/K_H	Gy^{-1}	10^{-1}	2.34	2.23	2.87
Temperature			41.90°	41.86°	41.86°

t_q=unperturbed quasi-threshold thermal dose
K_I=interaction coefficient
D_qI=interaction quasi-threshold radiation dose
t_qI=interaction quasi-threshold thermal dose.

The best fit parameters listed in Table I were used to calculate the survivals indicated by the solid lines through the data points of Figs. 1, 2 and 3.

The perturbed radiation sensititivies, K_R', for each hyperthermia exposure, and the perturbed thermal sensitivities, K_H', for each radiation dose were determined for each data set separately and averaged. K_R' and K_H' are the radiation sensitivities and the thermal sensitivities respectively for each individual survival curve determined under interaction conditions (see appendix to Loshek *et al.*, 1977a).

The radiation sensitivity curves, $K_R'=f(t)$, are illustrated in Fig. 4. It can be seen that the radiosensitivity increases with hyperthermia dose for all three types of radiation. The hyperthermia sensitivity curves, $K_H'=f(D)$, are illustrated in Fig. 5. Again, there is an approximately linear increase in thermal

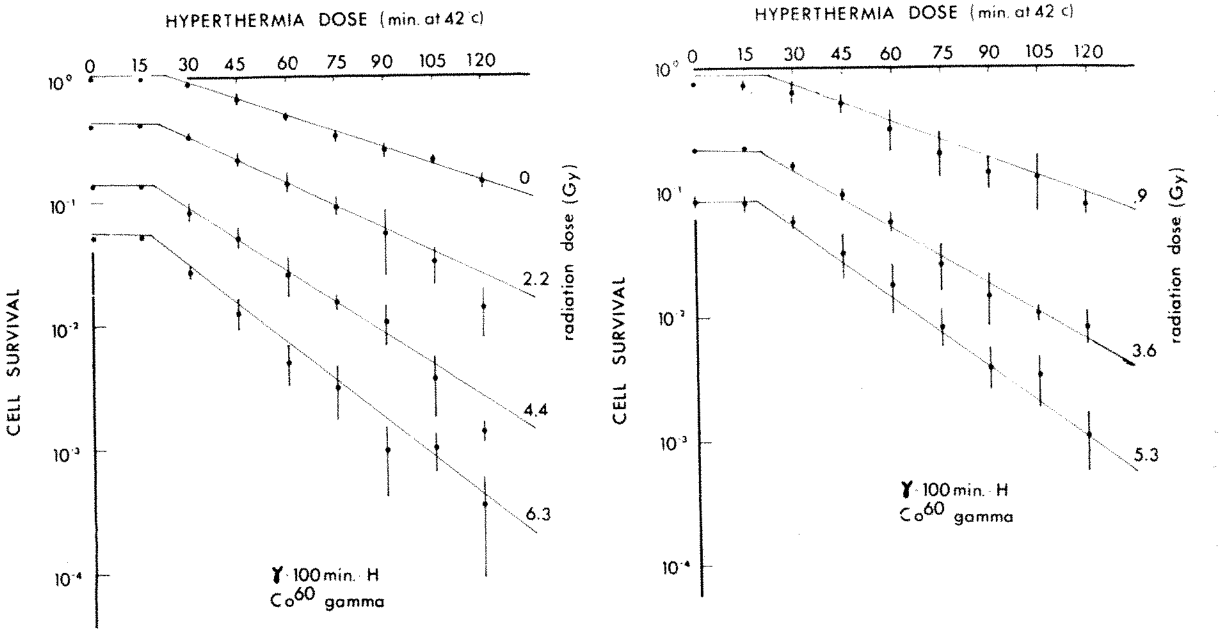


FIG. 2.

CHO cell survival as a function of hyperthermia dose 100 minutes after irradiation with ^{60}Co γ rays. Data points represent the mean and standard error for three observations.

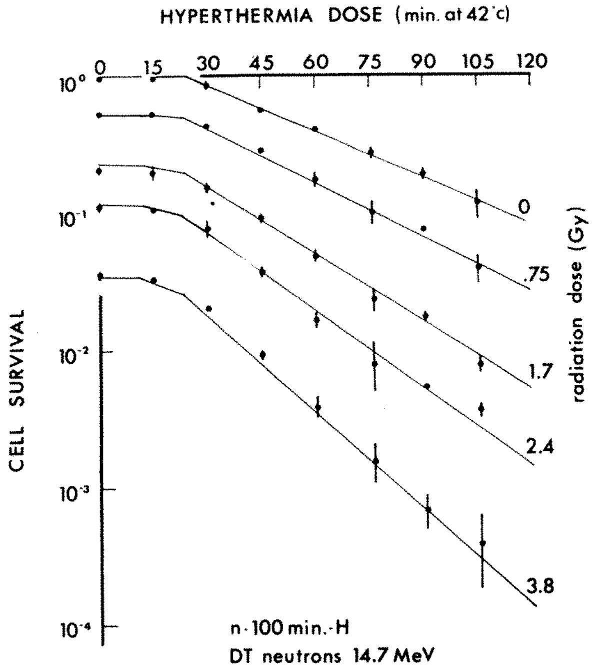


FIG. 3.

CHO cell survival as a function of hyperthermia dose 100 minutes after irradiation with 14.7 MeV neutrons. Data points represent the mean and standard error for three observations.

sensitivity with radiation dose. The solid lines drawn through the sensitivity curves are the sensitivities predicted using the parameters of Table I.

The slopes ($\partial K_R'/\partial t$ and $\partial K_H'/\partial D$) of the sensitivity curves provide independent estimates of the interaction coefficient. These data and the independent assessments of the unperturbed radiosensitivities and hyperthermia inactivation rates are listed in Table II.

DISCUSSION

The interaction observed for the neutron irradiation is qualitatively similar to that observed by Ngo *et al.* (1977) for 0.8 MeV neutrons using V79 cells. However, Hahn *et al.* (1976) observed primarily additive interaction for 3.5 MeV neutrons using an *in vivo* assay of effect on Ridgeway Osteogenic Sarcomas. Gerner and Leith (1977) also found a mainly additive interaction for high LET carbon ions and hyperthermia with respect to survival of CHO cells.

Comparison of the parameters K_R and K_H obtained for the interaction equation (1) with those obtained independently reveals no significant differences. The values of $\partial K_R'/\partial t$ and $\partial K_H'/\partial D$ are not significantly different for any one of the radiation qualities and the weighted mean, K_I, is not

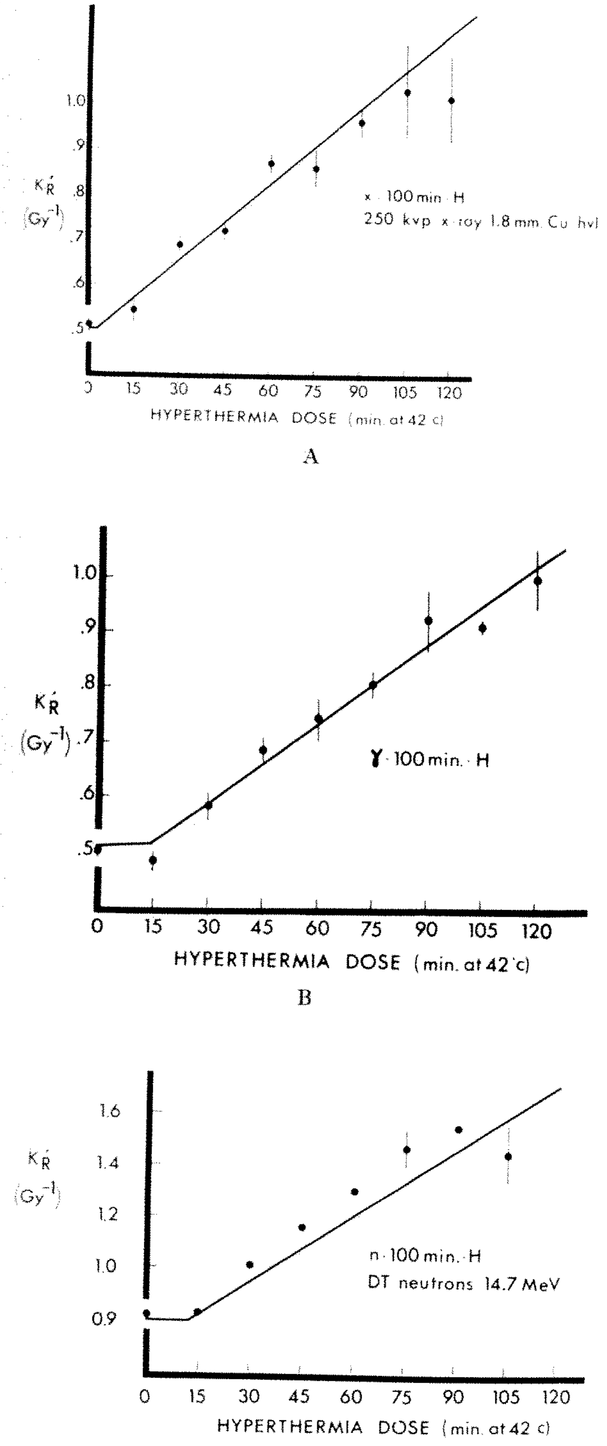


Fig. 4.

CHO cell radiosensitivity, K_R', as a function of hyperthermia dose, t. Data points represent the mean and standard error for three observations for (A) 250 kV X rays (B) ^{60}Co γ rays and (C) 14.7 MeV neutrons.

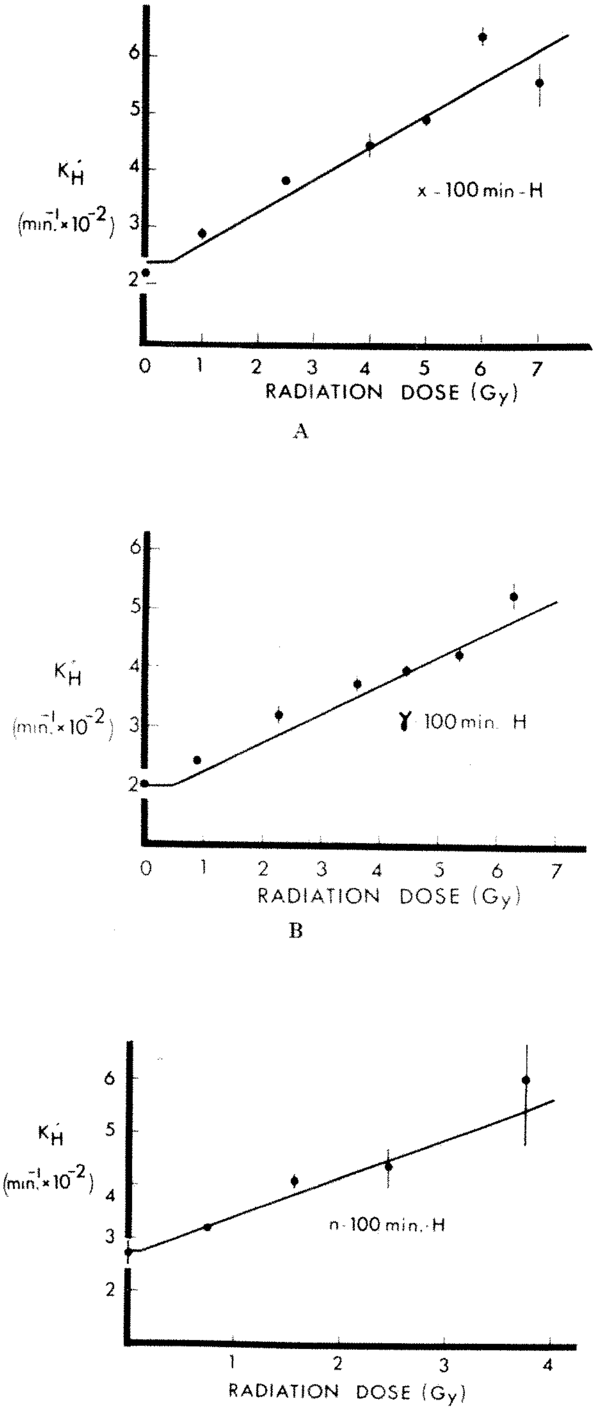


Fig. 5.

CHO cell thermal sensitivity, K_H', as a function of radiation dose, D. Data points represent the mean and standard error for three observations for (A) 250 kV X rays, (B) ^{60}Co γ rays and (C) 14.7 MeV neutrons.

significantly different from the value obtained for the survival surface, equation (1). Thus it is seen that for these three data sets, either method of analysis might be used.

There is a decrease in the interaction quasi-threshold dose, D_qI, for neutrons compared with X or γ radiation that parallels the change of the unperturbed quasi-threshold dose D_q. This similar response to a change in radiation quality suggests that D_q and D_qI characterize similar mechanisms. That is, just as D_q represents the repair or accumulation of unperturbed sublethal damage, the interaction quasi-threshold dose, D_qI, may represent the repair or accumulation of radiation-induced damage that is responsible for interaction. The amount of repair of interaction damage possible with neutrons would then be less than that possible with γ radiation. The values of K_R and K_I obtained for ^{60}Co and 250 kV X rays reveal no statistically significant differences. The neutron data exhibit both an increased radiosensitivity, K_R, and significantly larger values of the interaction coefficient, K_I, compared with those for the low LET radiation. However, the neutron experiments were performed several weeks before the γ and X-ray experiments and some change in the unperturbed hyperthermia sensitivity occurred. If the values of K_I are normalized to the values of K_H, it is found that the relative sensitization of thermal response, K_I/K_H, is still marginally higher for neutrons than X or γ rays as indicated in Table II. In the following discussion this discrepancy of thermal sensitivities will be ignored for simplicity, as it does not alter the general argument.

In order to explore the LET dependency of the interaction, a simple model of high-LET cell killing proposed by Katz *et al.* (1971) that is similar to other two-component models will be employed. It is postulated that cell survival can be described as a composite survival function due to two modes of inactivation, ion-kill and γ-kill. The ion-kill mode is caused by initial ionization and excitation due to primary particles and recoil protons. Survivors of the ion-kill mode are, according to the Katz theory, unaffected by ion-kill damage and only exhibit the damage due to the γ-kill component of the radiation. The ion-kill component is characterized by an exponential survival curve described as arising from a saturated multi-hit mechanism. The γ-kill mode due to δ rays associated with the primary and secondary interactions is characterized by a shouldered survival curve that would be representative of damage due to ^{60}Co γ radiation.

Before using the ^{60}Co data in an analysis of the neutron interaction data, it is necessary to discuss the possible effects of the difference in dose rates. If the ^{60}Co dose rate had been reduced to the dose rates corresponding to the lower neutron irradiations, the slope of the radiation survival curve, K_R, would have been expected to decrease somewhat due to concurrent repair of unperturbed radiation damage. The results of Railton *et al.* (1975) in split-dose experiments with the same cell line in CO_2 buffered Hams F10 at neutron dose rates of 0.10 and 0.60 Gy/min suggest that a small amount of repair of unperturbed neutron damage may be occurring at dose rates of about 0.10 Gy/min. So far as radiation damage responsible for interaction with hyperthermia is concerned, it has been shown that such damage is also capable of being repaired, since the interaction gradually disappears with increasing separation between the hyperthermia and radiation doses (Gerweck *et al.*, 1975). Accordingly, at low radiation dose rates a concurrent repair of damage responsible for interaction may take place, similar to that occurring with unperturbed damage, resulting in decreased values of the interaction coefficient, K_I. This suggestion is supported by the observations of Harisiadis *et al.* (1978) that, when V79 cells were irradiated at a dose rate of 0.036 Gy/min and subsequently heated for six hours at 41°C, the thermal enhancement ratios were lower than those observed for an acute radiation dose rate of 0.94 Gy/min. Thus the values of K_I and K_R obtained for ^{60}Co radiation may be appropriate as limiting upper values for low

TABLE II

Interaction parameter (independent) radiation—100 min—h

Parameter	Unit	Multiplying Factor	^{60}Co γ	250 kV X	14.7 MeV n
K_R	Gy^{-1}	10^{-1}	5.03 ± 0.14	5.15 ± 0.18	9.06 ± 0.02
K_H	min^{-1}	10^{-2}	2.04 ± 0.11	2.19 ± 0.09	2.72 ± 0.27
$\partial K_R'/\partial t$	$Gy^{-1}min^{-1}$	10^{-3}	5.08 ± 0.31	4.78 ± 0.46	7.13 ± 0.90
$\partial K_H'/\partial D$	$Gy^{-1}min^{-1}$	10^{-3}	4.64 ± 0.45	5.03 ± 0.61	8.60 ± 1.14
K_I	$Gy^{-1}min^{-1}$	10^{-3}	4.94 ± 0.45	4.87 ± 0.61	7.70 ± 1.14
K_I/K_H	Gy^{-1}	10^{-1}	2.42 ± 0.26	2.22 ± 0.29	2.83 ± 0.51

LET radiation associated with the neutron irradiations.

An analysis of previous ^{60}Co and DT neutron data on the same cell line, carried out at this Institute (Railton *et al.*, 1975; Katz and Sharma, 1974), indicated that about 25% of the total neutron dose was expended in the ion-kill mode. If it is assumed that the interaction is due to the γ-kill component only, and that the γ-kill component is similar to that observed for the γ-kill component of 1 MeV photons, the interaction coefficient for neutrons should be equal to or less than 0.75×0.00494 Gy^{-1}min^{-1}= 0.00371 Gy^{-1}min^{-1}, whereas the observed coefficient is nearly twice this value. If significant repair is taking place at the lowest neutron dose rates, a similar argument can be applied to the actual increases in K_H' at 4 Gy from neutrons and 3 Gy from γ radiation. This sensitization, therefore, cannot be due to a purely γ-type radiation effect at the estimated fraction of γ-kill, or indeed at any fraction of γ-kill.

There exist two possibilities: (1) the fraction of the dose expanded in ion-kill increases with increasing hyperthermia dose; and (2) the ion-kill component takes part in the interaction.

If the sensitizing effect of hyperthermia were to shift damage progressively from the γ-kill to the ion-kill mode, this could explain the observation. However, it is difficult to maintain the concept of the initial spatial distribution of energy as the basis for distinguishing the type of radiation damage, if the categorization of radiation damage is to be controlled by the hyperthermia dose, particularly when the hyperthermia exposure occurs after the radiation exposure.

Thus, it is concluded that, if no reasonable value of the γ-kill fraction will allow the observed sensitization to be attributed solely to the γ-kill fraction, the ion-kill component must take part in the interaction. The only mechanism that can be envisaged for sensitization of the ion-kill component would be that in addition to those cells receiving ion-kill lethal damage, a number of surviving cells, proportional to those actually killed, receive damage which can be converted to lethal damage by hyperthermia, but which cannot interact with the low-LET component of radiation as sublethal damage.

If an RBE for interaction is expressed as the ratio of the neutron and γ interaction coefficients, this would be at most $0.00770/0.00494 = 1.56$. When this is compared with the ratio of the radiosensitivities $0.906/0.503 = 1.80$, it appears that the interaction component is less sensitive to an increase in LET. However, it can be demonstrated that the deposition of radiation-induced interaction damage is not necessarily less dependent on LET than the normal component of radiation damage.

Let

G = probability of kill due to the unperturbed effects of a γ-radiation dose D,

G_I = probability of kill due to the interaction events arising from a γ-radiation dose D and a hyperthermia exposure t,

N = probability of kill due to the unperturbed effects of a neutron radiation dose D,

N_I = probability of kill due to the interaction events arising from a neutron radiation dose D and a hyperthermia exposure t,

then $(1-G)$ is the probability of a cell surviving the unperturbed γ-dose D and $(1-G)G_I$ is the probability of cell killing due to γ and hyperthermia interaction events. Similarly, $(1-N)N_I$ is the probability of cell killing due to neutron and hyperthermia events. The ratio N/G is approximately the RBE for unperturbed cell killing. The ratio N_I/G_I is approximately the RBE for the deposition of radiation-induced interaction events. The ratio $(1-NN_I/(1-G)G_I$ is the RBE for expression of interaction and is always less than N_I/G_I whenever N/G is greater than one. Thus, the apparent RBE for interaction is reduced over the actual ratio of probabilities for depositing interaction-type damage by the increased RBE for the unperturbed system. The probability per unit dose of radiation-induced interaction damage may therefore be as sensitive to changes in LET as the probability of damage leading to unperturbed cell killing. It would also appear likely that the interaction RBE will continue to increase with LET up to an LET at which the increased radiochemical yield of interaction-type damage is balanced by the decreased probability of a cell surviving the unperturbed effects of the radiation dose. For LETs higher than this, the interaction RBE will decrease with increasing LET, until the interaction RBE is zero. In the context of target theory, the radiation induced interaction damage targets must be sufficiently remote from a target that would be vulnerable to lethal damage due to a single high-LET event alone.

This phenomenon may explain the results of Gerner and Leith (1976) who observed a marginal synergistic interaction between hyperthermia and accelerated carbon ions with an LET substantially higher than that for 14.7 MeV neutrons. An analysis similar to the above reveals that, for radiations with RBEs less than one, the expression of synergistic interaction is enhanced by the decreased RBE over that of the reference radiation. This may in part be the explanation for the enhanced hyperthermia interaction observed for 15 MeV electrons compared to 200 kV X rays, as observed by Schrader-Reichhardt and Markus (1978).

CONCLUSION

Interaction between hyperthermia and radiation has been demonstrated to exist for 250 kV X rays, ^{60}Co γ and DT neutron radiation. The relation of interaction damage to radiation dose and radiation quality is shown to be similar to that for the unperturbed radiation dose. It is concluded that high LET radiation contributes radiation-induced interaction damage with an LET dependency similar to that of the radiation damage responsible for unperturbed cell killing. It is also suggested that this high-LET interaction damage is affected, but to a lesser degree than low-LET interaction damage, by a mechanism of repair or accumulation of damage similar to the mechanism responsible for the shoulder of the unperturbed survival curve.

ACKNOWLEDGMENT

We are glad to acknowledge both the assistance with the neutron irradiations and many valuable discussions with Doctors R. C. Lawson and D. P. Porter of the Department of Clinical Physics and Bio-Engineering, West of Scotland Health Boards.

REFERENCES

BELLI, J. A. and BONTE, F. J., 1963. Influence of temperature on the radiation response of mammalian cells in culture. *Radiation Research, 18*, 272–276.

BEN HUR, E., BRONK, B. V. and ELKIND, M. M., 1972. Thermally enhanced radiosensitivity of cultured Chinese hamster cells. *Nature, 238*, 209–211.

BEN HUR, E., ELKIND, M. M. and BRONK, B. V., 1974. Thermally enhanced radioresponse of cultured Chinese hamster cells. Inhibition of repair of sublethal damage and enhancement of lethal damage. *Radiation Research, 58*, 38–51.

DENNIS, J. A., 1971. Energy loss characteristics of heavy ions in nitrogen, carbon dioxide, argon, hydrocarbon gases and tradescantia tissue. *AERE-M 2346*.

GERNER, E. W. and LEITH, J. T., 1977. Interaction of hyperthermia with radiations of different linear energy transfer. *International Journal of Radiation Biology, 31*, 283–288.

GERWECK, L. E., GILLETTE, E. L. and DEWEY, W. C., 1975. Effect of heat and radiation on synchronous Chinese hamster cells: killing and repair. *Radiation Research, 64*, 611–623.

HAHN, E. W., CANADA, T. R., ALFIERI, A. A. and MCDONALD, J. C., 1976. The interaction of hyperthermia with fast neutrons or X rays on local tumor response. *Radiation Research, 68*, 39–56.

HARISIADIS, L., SUNG, D., DESSARIS, N. and HALL, E. J., 1978. Hyperthermia and low dose rate irradiation. *Radiology, 129*, 195–198.

HENLE, K. J. and LEEPER, D. B., 1976. Interaction of hyperthermia and radiation in CHO cells: recovery kinetics. *Radiation Research, 66*, 505–518.

ICRU REPORT 13, 1969. Neutron fluence, neutron spectra and kerma. (International Commission of Radiation Units and Measurements, Washington, DC, USA).

KATZ, R., ACKERSON, E., HOMAYOONFAR, M. and SHARMA, S. C., 1971. Inactivation of cells by heavy ion bombardment. *Radiation Research, 47*, 402–425.

KATZ, R. and SHARMA, S. C., 1974. Cellular survival in a mixed radiation environment. *International Journal of Radiation Biology, 26*, 143–146.

LOSHEK, D. D., ORR, J. S. and SOLOMONIDIS, E., 1977a. Interaction of hyperthermia and radiation: the survival surface. *British Journal of Radiology, 50*, 893–901.

1977b. Interaction of hyperthermia and radiation: temperature coefficient of interaction. *British Journal of Radiology, 50*, 902–907.

1978. Interaction of hyperthermia and radiation: survival model. In *Cancer Therapy by Hyperthermia and Radiation*, pp. 211–213. Ed. C. Streffer *et al.* (Urban and Schwarzenberg, Baltimore/Munich).

NGO, F. Q. H., HAN, A., UTSUMI, H. and ELKIND, M. M., 1977. Comparative radiobiology of fast neutrons: relevance to radiotherapy and basic studies. *International Journal of Radiation Oncology, Biology and Physics, 3*, 187–193.

RAILTON, R., LAWSON, R. C. and PORTER, D., 1975. Interaction of X rays and neutron effects on the proliferation capacity of Chinese hamster cells. *International Journal of Radiation Biology, 27*, 75–82.

ROBINSON, J. E. and WIZENBERG, M. J., 1974. Thermal sensitivity and the effect of elevated temperatures on the radiation sensitivity of Chinese hamster cells. *Acta Radiologica, 13*, 241–248.

SCHRADER-REICHHARDT, U. and MARKUS, B., 1978. The effectivity of hyperthermia combined with high energy electrons and X rays. In *Cancer Therapy by Hyperthermia and Radiation*, pp. 206–208. Ed. C. Streffer *et al.* (Urban and Schwarzenberg, Baltimore/Munich).

1981, *British Journal of Radiology*, 54, 48–50

Technical notes

Angiography assisted by a new videostore system

By R. S. Dossetor, F.R.C.R.,
Hurstwood Park Neurological Centre, Haywards Heath, Sussex
B. Keane, M.Inst.P.,
Department of Medical Physics, Royal Sussex County Hospital, Brighton, Sussex
R. D. Jeffrey and J. Pressburger, B.Sc.
Thermal Controls Ltd., Hove, Sussex

(Received February 1980 and in revised form June 1980)

A new videostore system which has been developed in conjunction with Thermal Controls Ltd. enables television images made during X-ray intensifier fluoroscopy to be stored and then superimposed in subtraction on live fluoroscopy images. For angiography the system is used in the following way. First, contrast is injected through the catheter and the resulting image stored (Fig. 1A). After this, live fluoroscopy provides a subtracted image of the vessel system. It is then easier to guide the catheter into the

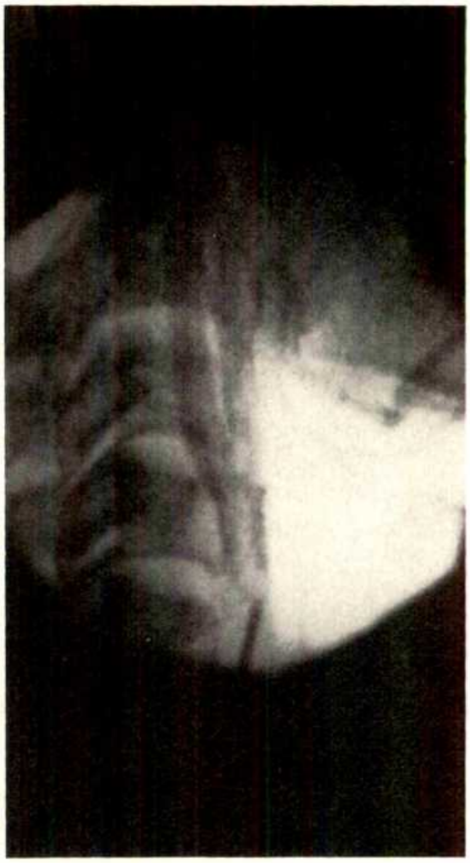


FIG. 1A.
Stored image after injection of contrast into the left common carotid artery.

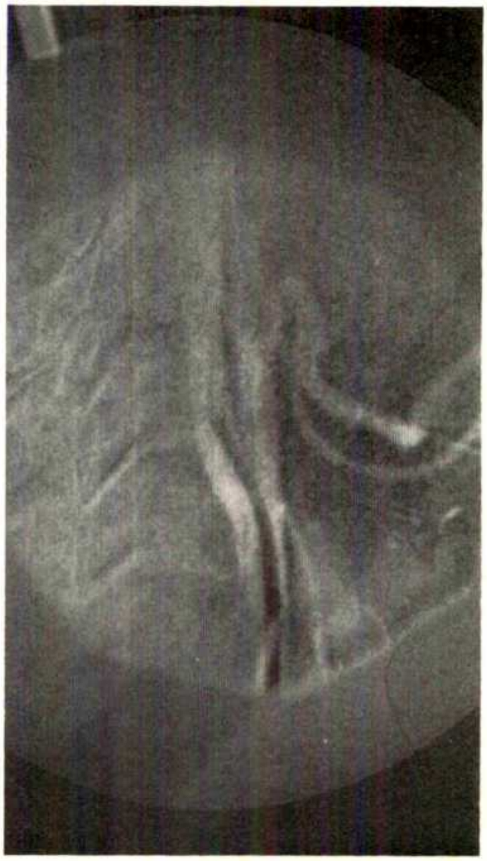


FIG. 1B.
The catheter is guided into the internal carotid artery using the displayed map of the vessels as a guide.

right vessel as a map of the vessel system is displayed on the screen during fluoroscopy (Fig. 1B). The use of subtraction assists arterial visualization when there are complex overlying structures (Fig. 2A, 2B).

The image is recorded by writing it as a raster in an electrostatic storage tube such as those commonly used for graphic effects in television communications systems. Once written, the frame can be read out many times with negligible fading over many minutes; in effect it acts as if it were another TV camera looking at a fixed image. We now have the moving image signal from the image intensifier and the fixed image signal from the videostore. It is a relatively simple matter to add the two signals in a summing amplifier and the combined signal then appears on the monitor as one image. When one of the signals is passed through an inverting amplifier (it is at the user's choice which this is), that signal appears in the negative phase and the combined result is subtraction.

DISCUSSION

This system has a number of new features which facilitate its use.

1. Each image stored consists of a number of frames integrated together to increase the signal-to-noise ratio. This results in a much improved image compared with other systems which use only a single relatively noisy frame. This is a unique feature of the system.

2. A special footswitch is provided giving heel and toe operation of the videostore and X-ray machine, either independently or combined. The operator can then choose his technique to maximize the viewing time of stored images and minimize the viewing time of live fluoroscopy. This is also a unique feature.

3. Whereas earlier workers (Pfieler and Haendle, 1975; Damascelli *et al.*, 1977; Reismann, 1979) used a magnetic disc store or tape recorder to which the rest of the equipment had to be synchronized, the present method uses an electron tube store which

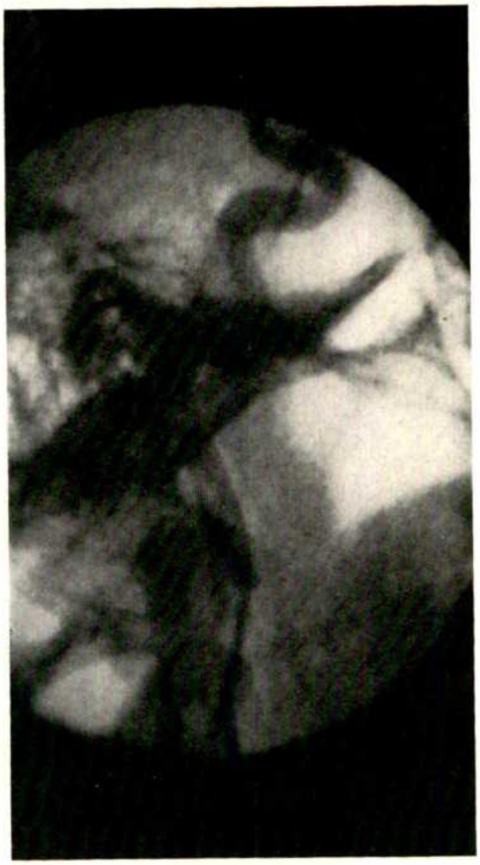
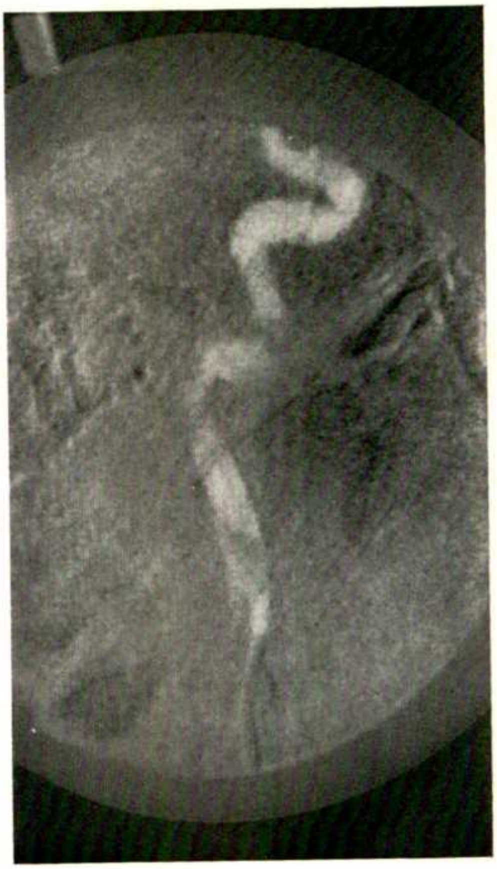


FIG. 2A.
Stored image of left internal carotid artery after injection of contrast.



2B.
Subtracted image of left internal carotid artery obtained by live fluoroscopy.

1981, *British Journal of Radiology*, *54*, 50–53

can adapt itself to the existing CCTV operating conditions.

4. The system enables quicker identification of significant features in the stored image and reduces the fluoroscopy "on" time to carry out a given manipulation.

Note: All the figures have been photographed direct from the TV monitor.

APPLICATIONS

This technique has potential applications in assisting difficult catheterizations, in interventional radiology and in angiography training. In all of these situations the method can be used to reduce the time of the procedure, the amount of contrast used and the radiation dose.

REFERENCES

PFIELER, M. and HAENDLE, J., 1975. State of the art and development tendencies of X-ray image intensifier TV systems. *Electromedica*, No. 5, pp. 152–155.

DAMASCELLI, B., MUSMECI, R., PROSPERINI, G., SPAGNOLI, I. and USLENGHI, C., 1977. Selective and superselective angiography of the head and neck region. *Electromedica*, No. 1, pp. 21–25.

REISMANN, B., 1979. The intra-operative use of the X-ray television chain with videorecorder—a contiibution to a reduction of the radiation exposure and improvement in diagnostic reliability. *Electromedica*, No. 1, pp. 15–17.

Factors affecting the breathing rate of mice as used for studies of radiation damage to lungs

By E. L. Travis, Ph.D*., J. D. Down†, L. Hall, F.I.A.T., B. Vojnovic, M.Sc. and S. J. Holmes, B.Sc.

Gray Laboratory of the Cancer Research Campaign, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

(*Received April 1980 and in revised form June 1980*)

Breathing rate is a useful parameter for evaluating lung function in mice after various treatment procedures which may damage the lung, including radiation doses relevant to radiotherapy. It can be measured by non-invasive, non-destructive methods, thus allowing quantitative assessment of lung changes in the same mouse over a period of time (Travis *et al.*, 1979). The method is being used regularly to assay early and late changes after irradiation of the whole lung as well as drug-induced lung injury (Travis *et al.*, 1979; 1980; Collis *et al.*, 1980).

A wide range of measured values of normal breathing rates in undisturbed mice has been reported. Rates as low as 109 breaths per minute (BPM) (Crosfill and Widdicombe, 1961) and as high as 230 BPM have been reported (Guyton, 1947; Spector, 1956). In a study of changes in breathing rate after X-irradiation of both lungs, we measured a mean rate of 330 BPM in control, unirradiated male CBA mice during quiet respiration. Because this rate was higher than the previously reported values in mice, we carried out a series of experiments in unirradiated mice to answer the following questions.

(1) Was the apparently high breathing rate observed by us in CBA mice an artefact of our testing system?
(2) How much did breathing rate depend on the strain and sex of the mice?
(3) Was there a correlation between breathing rate and relative lung weight in different strains of mice?

APPARATUS AND METHODS

A whole-body mouse plethysmograph was used for measuring breathing rate (Travis *et al.*, 1979). Briefly, the system consisted of a clear Perspex air-tight chamber with an internal volume of 125 ml. One end of the chamber was fitted with a microphone modified to act as an electrical capacitance manometer, thus converting pressure changes in the chamber into an electrical signal. The resulting signal was electronically processed and the rate of pressure changes in the chamber was recorded on a pen trace. The rate signal was calibrated over a range of known frequencies enabling the reading on the chart paper to be converted to Hz (cycles/s) which corresponded to breaths/second.

The breathing rate of ten CBA male mice, measured at fortnightly intervals over a period of one year, ranged from 310 to 355 BPM with an average breathing rate of 328 BPM (Fig. 1). Although a small but just significant decrease in breathing rate was observed with age ($p < 0.05$), even the values at one year were higher than values published in the literature.

Present addresses: *National Cancer Institute, Radiation Oncology Branch, Bldg 10, Rm B3B38, Bethesda, Maryland 20205, USA.

†Institute of Cancer Research, Sutton, Surrey SM2 5PX.

The breathing rate of CBA mice obtained using the plethysmograph was checked by two other methods. One technique was based on the temperature difference between inhaled and exhaled air. Thermistors were inserted in a nose cone which was placed over the snout of a CBA mouse which had been trained to accept it while being gently held in the hand. The number of temperature cycles per second was recorded on an oscilloscope. The breathing rate measured by this technique was 300 BPM, in precise agreement with the value obtained with the plethysmograph for this mouse. The breathing rate was further checked by ciné filming of a "trained" CBA mouse in the plethysmograph while simultaneously recording breathing rate on the pen recorder.* The respiratory movements of the rib cage were clearly visible when the film was projected in slow motion and counted by 12 observers. The number of thoracic movements counted varied between individual observers from 310 to 340 per minute which agreed well with the value of 336 BPM obtained from the pen recorder.

The breathing rate of unstressed, unrestrained, CBA mice was consistently within the range 300 to 345 BPM regardless of the measurement technique. It appears then that the breathing rate of this mouse strain is higher than previously reported values for mice and that the values are not an artefact of our testing system.

Biological factors

The decrease in breathing rate as a function of age (Fig. 1) is a consistent finding and could be due either to a true age related change or to acclimatization of the mice to the chamber, *i.e.* training. Aging has been reported to cause an increase in breathing rate (Mauderly, 1974). Training is a more likely influence on breathing rate in our system. Although the mice did not appear to be stressed in the chamber at any time, they were calmer in the chamber after the 20-week testing time, suggesting that training slightly influences the breathing rate. What is important is that control mice should always be tested at the same time as experimental mice.

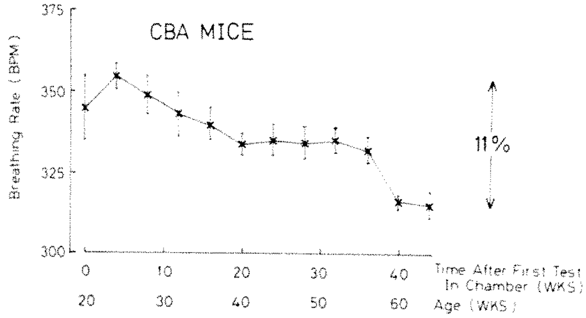


FIG. 1.

Breathing rate of male CBA mice tested at monthly intervals for one year. Each point represents the mean ±1 SEM. The breathing rate decreased with age or with acclimatization to the procedure.

The plethysmograph is large enough to permit a 25–30 g mouse to move freely in the chamber. It was found that restraining a mouse by holding gently in the hand reduced its breathing rate by about 10%. The breathing rates of three "trained" CBA mice were measured under standard testing conditions in the chamber. Each mouse was then placed in a wire mesh tube which restricted all movement. The mouse in the restrainer was placed in the plethysmograph and breathing rate recorded. Physical restraint reduced the breathing rate of the mice by 20%. What cannot be determined is whether restraint stressed the CBA mice and thus caused their breathing rate to fall in some unexpected way, or whether the restriction of movement allowed the breathing rate to be recorded during true quiet respiration. The CBA mice did, however, appear to be comfortable and relaxed in the chamber when unrestrained. Clearly the conditions of testing and handling of the mice can affect breathing rates and must be carefully controlled and uniformly maintained.

A concentration of 5% CO_2 is known to stimulate breathing rate in many species (Green, 1968). Because the plethysmograph was an airtight chamber, accumulation of expired CO_2 could cause this value to be exceeded within several minutes. The concentration of O_2 in the chamber was measured in a paramagnetic oxygen meter at timed intervals up to five minutes for seven of the "trained" CBA mice. The breathing rate was recorded simultaneously. The reduction in oxygen concentration of the respired gas after two minutes, the normal testing time, was measured as 4% (Fig. 2). Although CO_2 was not measured, it is reasonable to assume that the amount of CO_2 produced by a mouse during breathing in a closed chamber does not exceed the O_2 consumed. Therefore, in two minutes, no more than 4% CO_2 would be accumulated in the chamber, probably somewhat less, and the O_2 concentration would have fallen to 16%.

The breathing rate did not rise during this time, remaining stable up to three minutes of testing;

---

*Locam Camera, Ektachrome 7242, *f*5.6; film speed, 100 frames per second; viewed on 16 mm projector at silent speed, thereby reducing the speed by four.

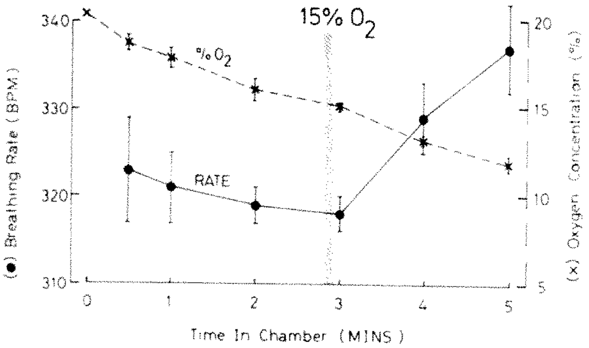


FIG. 2.

Oxygen concentration (×) and breathing rate (●) for animals kept in a closed plethysmograph for varying lengths of time. Each point represents the mean ±1 SEM for seven CBA male mice.

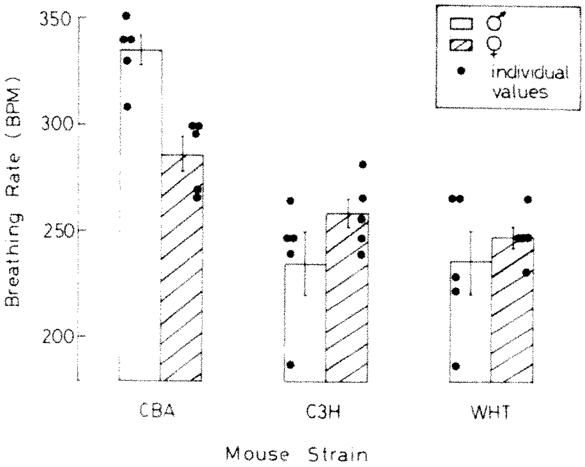


FIG. 3.

Breathing rates for male and female mice of three different inbred strains. Points represent individual animals; the error bar is 1 SEM for each group of five mice.

TABLE I

RATIO OF LUNG WEIGHT TO TOTAL BODY WEIGHT IN TWO MOUSE STRAINS

Group	Body weight (g)	Lung weight (g)	Lung wt./Body wt.	Breathing rate (BPM)
CBA/Ht (5)				
Mean	32.453	0.135	0.004	330
SEM	1.226	0.002	0.0001	
WHT/Ht (5)				
Mean	35.313	0.175	0.005	248
SEM	0.996	0.007	0.0002	

indeed, a slight decrease was observed (Fig.2). It appears, therefore, that the high breathing rates measured in CBA mice in the plethysmograph are not due to an increase in CO_2 in the chamber during the normal two minutes testing time. However, after three minutes of testing the breathing rate increased by 6%, as the oxygen concentration fell below 15% and the concentration of CO_2 in the chamber rose above 5%. This level of CO_2 would indeed be expected to stimulate breathing (Green, 1968). The mice also exhibited agitation and stress after three minutes, signs which are suggestive of anoxia and hypercapnia.

Previous publications on breathing rates of mice do not state the strain or sex (Crosfill and Widdicombe, 1961; Guyton, 1947; Spector, 1956). Breathing rates were measured in our plethysmograph in five mice of each sex of the three mouse strains held in the Gray Laboratory, CBA/Ht, WHT/Ht and C3H/He. All these mice were three months old and were not "trained". Breathing rate was clearly strain-dependent (Fig. 3). Both sexes of the CBA strain had a significantly higher rate than either the C3H or WHT strain ($p<0.01$ in the males and $p<0.05$ in the females). The breathing rates measured for the C3H and WHT strains were close to the upper limits of previously reported values, 235 and 237 BPM respectively. There was a clear sex dependence of breathing rate in the CBA strain only, the males having a 15% higher rate than the females ($p<0.01$). These results stress the importance of stating the strain of mice tested.

Another factor which could influence breathing rate is the size of the lungs relative to the total body (Agostoni *et al.*, 1959). The breathing rate of six untrained male CBA and five male WHT mice, six months old, was measured in the plethysmograph and the mice were then weighed and killed by ether anaesthesia. The lungs were rapidly removed from the thorax, cut from the bronchus, blotted and weighed. The ratios of wet lung weight to body weight in the two strains indicated that the CBA mice have lungs about 18% smaller than those of WHT mice (Table I). The breathing rate of the CBA mice was 38% higher than in the WHT males. The higher breathing rate in the CBA mice may be necessary to compensate partially for the relatively small lung size in these mice.

ACKNOWLEDGMENTS

The authors wish to thank Mr. B. Hall for filming the mouse in the plethysmograph, Dr. B. D. Michael for assistance with the O_2 measurements, and Prof. J. F. Fowler, Dr. J. Denekamp and Dr. B. D. Michael for many helpful discussions. We also thank Mr. F. W. Butcher and Miss A. E. Marriott for care and maintenance of the mice and Mrs.

C. A. Hartz and Mrs. G. F. Mason for secretarial assistance. We are grateful to the Cancer Research Campaign for funding the study.

REFERENCES

AGOSTONI, E., THIMM, F. F. and FENN, W. O., 1959. Comparative features of the mechanics of breathing. *Journal of Applied Physiology*, *14*, 679–683.

COLLIS, C. H., WILSON, C. M. and JONES, J. M., 1980. Cyclophosphamide-induced lung damage in mice: protection by a small preliminary dose. *British Journal of Cancer*, *41*, 901–907.

CROSFILL, M. L. and WIDDICOMBE, J. G., 1961. Physical characteristics of the chest and lungs and the work of breathing in different mammalian species. *Journal of Physiology*, *158*, 1–14.

GREEN, J. H., 1968. *An Introduction to Human Physiology*, (2nd ed.), pp. 51–63 (Oxford University Press, London).

GUYTON, A. C., 1947. Measurement of the respiratory volume of laboratory animals. *American Journal of Physiology*, *150*, 70–77.

MAUDERLY, J. L., 1974. Influence of sex and age on the pulmonary function of the unanaesthetized beagle dog. *Journal of Gerontology*, *29*, 282–289.

SPECTOR, W. S., 1956. *Handbook of Biological Data*, p.267 (W. B. Saunders, Philadelphia).

TRAVIS, E. L., VOJNOVIC, B., DAVIES, E. E. and HIRST, D. G., 1979. A plethysmographic method for measuring function in locally irradiated mouse lung. *British Journal of Radiology*, *52*, 67–74.

TRAVIS, E. L., DOWN, J. D., HOLMES, S. J. and HOBSON, B., 1980. Radiation pneumonitis and fibrosis in mouse lung assayed by respiratory frequency and histology. *Radiation Research*, *84* (*in press*).

Induced radioactivity in patients from betatron irradiation

By G. W. Bennett, Ph.D. and R. Dobert.

Brookhaven National Laboratory, Upton, New York 11973

J. Meltzer, M.D.

Nassau County Medical Center, State University College of Medicine at Stony Brook, East Meadow, New York 11554

B. E. Archambeau, M.D.

University of Chicago, Chicago, Illinois 60606

and J. O. Archambeau, M.D.

City of Hope National Medical Center, Duarte, California 91010, USA

(*Received January 1980 and in revised form July 1980*)

The nuclear binding energy averages 7–8 MeV per nucleon. If a nucleus is penetrated by a quantum of energy which exceeds this average binding energy, the nucleus may lose one or more of its nucleons. The residual nucleus may be radioactive. As early as 1949, induced radioactivity in tissue from a 24 MeV synchrotron was demonstrated by Mayneord *et al.* (1949). This induced radioactivity results from the nuclear photo-effect and accounts for less than 1% of the total energy absorbed from a bremsstrahlung spectrum whose average energy is 10 to 15 MeV (Joyet, 1965). Since this correlates with energy levels used clinically in betatron irradiation, the induced activity may be useful in clinical applications, including correlation of the activity distribution and ultimately the dose distribution with that prescribed by the clinician. A similar visualization procedure for a therapeutic proton beam has been demonstrated using an on-line positron camera (Bennett *et al.*, 1978).

MATERIALS AND METHODS

The 33 MeV Brown Boveri betatron at Montefiore Hospital and Medical Center was utilized for this research in a clinical setting. Patients already undergoing radiation with standard treatment fields and fractionation schedules of 200–300 cGy (rad) were randomly selected for measurements of induced radioactivity.

Immediately after treatment the patient was brought to an enclosed area adjacent to the betatron room. A sodium iodide crystal was positioned on each side of a movable bed on which the patient rested (Fig. 1). By moving the bed it was possible to vary the position of the treatment field relative to the sensitive volume of the detector pair. The detectors were separated by 65–70 cm and were connected to discriminators with threshold just below the photopeak for annihilation radiation. Fast coincidences were fed to a multichannel analyser in multi-scaling

---

Supported by grant CA-188347 from the National Institutes of Health and United States Department of Energy under Contract No. EY-76-C-02-0016.

Address for reprints: J. Meltzer, M.D., Division of Radiooncology, Atlantic City Medical Center, 1925 Pacific Avenue, Atlantic City, N.J. 08221, USA.

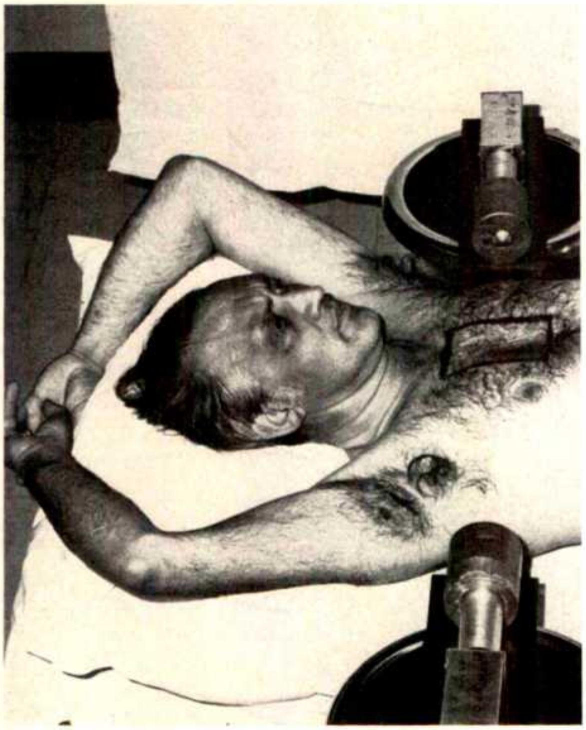


Fig. 1.
Photograph showing positioning of detectors.

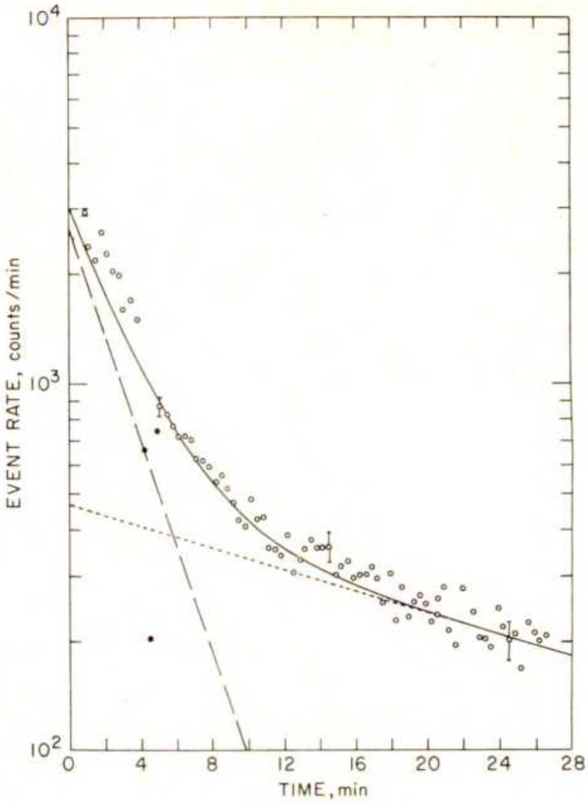


Fig. 2.
Decay of positron-emitting activity induced in pelvic region. The solid points represent measurements after the patient had moved.

mode with 20-second channel advance. Accidental coincidences were monitored at intervals. Detectors were carefully aligned for co-linearity and tested with a point source on the axis of the pair of detectors before the patient was positioned in the apparatus.

Originally, an effort was made to record on-line measurements of the patient in the betatron room. However, the high level of background activity made this impractical. For this reason, measurements were made outside the treatment room.

In three cases the detector crystals were 2.5 cm in diameter and 2.5 cm long. Event rates were measured repeatedly through the centre of the field, and at various distances outside the irradiated field. In the fourth case the crystals were 5 cm in diameter and 5 cm long. The patient was maintained in one position, to determine the event rate versus time.

Results

The activity within the irradiated volume in two pelvic irradiations, parallel-opposed fields with 180 and 200 cGy (rad) total dose, and one anterior mediastinum field, 200 cGy total dose, showed initial rates of 120 to 285 detected events per minute. The activity detected 2 to 25 cm from the edge of the irradiated volume was 0 to 12 coincidences per minute. The average ratio of event rate outside the treatment volume to the rate within the volume, corrected for decay, was 0.2 ± 0.07 for these three patients. None of the data are corrected for accidental coincidences; the accidental (delayed) coincidence rate was typically less than 14% of the prompt coincidence rate.

Figure 2 shows the measurements from the fourth patient, an anterior pelvic field. The field was a 15×16 cm diamond receiving 200 cGy given dose and 162 cGy tumour dose at mid-line. The scintillation crystals were 5 cm in diameter and 5 cm long. The initial recording delay of one minute represents the time to bring the patient from the betatron to the recording apparatus. The sharp dip in counts at 4.5 minutes resulted from movement of the patient so that the detectors were 2 cm beyond the edge of the field. The patient was then repositioned. The rapid fall-off of activity at the border of the treatment volume emphasizes the localization of the

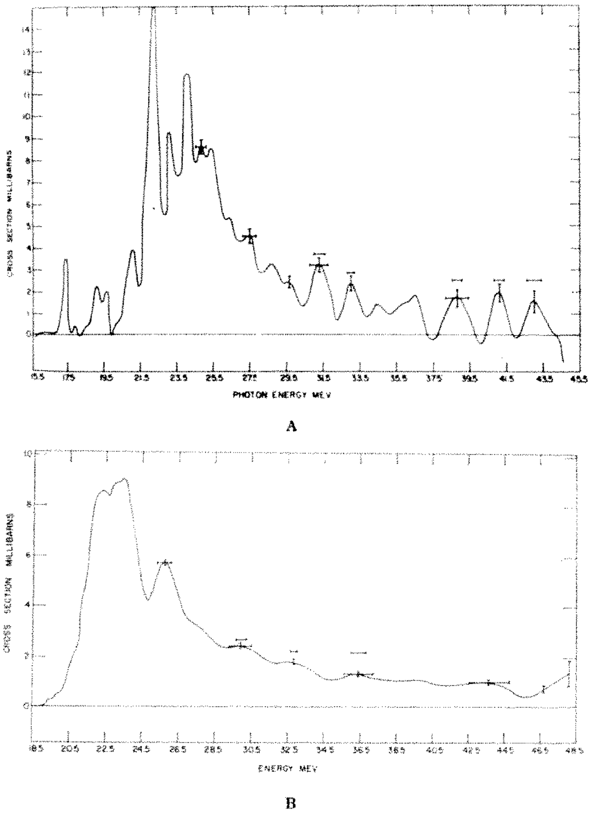


FIG. 3.

Excitation functions for the (γ, n) reaction (Cook *et al.*, 1966). (A) Oxygen. (B) Carbon.

induced activity to the treatment field. The ratio of event rate, corrected for decay, outside the field to the rate within the field was 0.17 ± 0.02. The delayed (accidental) coincidence rate during the first two minutes of data acquisition averaged 16%.

The data after this patient was repositioned ($t > 5$ min) were fitted by least squares to a sum of exponentials. A component with half-life of two minutes (^{15}O) was evident with initial activity of $2.7 \pm 0.5 \times 10^3$ counts per minute, and a component with half-life of 20.4 minutes (^{11}C) was determined with initial activity of $4.7 \pm 0.6 \times 10^2$ counts per minute. A negligible initial activity, 27 ± 140 counts per minute, was assigned to ^{13}N, half-life ten minutes. Chi square for these results was 46.6 for 59 degrees of freedom.

DISCUSSION

The primary mechanism for production of activity *in vivo* from betatron irradiation is the photo-nuclear effect. In this reaction a γ ray removes a neutron from an atomic nucleus. The major components of tissue contributing to this interaction are ^{16}O (61% of body weight) and ^{12}C (23% body weight) (Snyder *et al.*, 1975). The excitation functions for these reactions are shown in Fig. 3. Threshold energies are 16.3 and 18.6 MeV respectively, with broad peaks occurring at 20–24 MeV. The element next in abundance in tissue, hydrogen, comprises 10% by weight but does not contribute a useful product. Other elements, including nitrogen (2.5% by weight), produce negligible activity compared with oxygen and carbon.

A potential application of this phenomenon is quality control in betatron radiation therapy, for machines with energy above the reaction threshold. The distribution of positron-emitting nuclei produced by the therapeutic beam can be measured by placing the patient in a suitable positron detector, *e.g.* a planar positron camera.

Surface fiducials may be referenced in the positron scintigrams and in cardiographs or CT scans by incorporating a point positron-emission source in a radio-opaque marker. By using a pair of such fiducials, proper registration and unity relative magnification of scintigram and radiograph are easily accomplished, permitting correlation of the activity distribution with anatomical landmarks.

The sensitivity of this technique using a positron camera may be determined by extrapolating the data of Fig. 2. The sensitive volume of the detector pair was 2 cm in diameter (full width at half maximum). A planar positron camera with 39 cm effective diameter, at the same separation but with a 2.5 cm thick crystal would have approximately 75 times the present sensitivity using only photopeak–photopeak coincidences, and 600 times if Compton–photopeak coincidences are included, at a small degradation in spatial resolution. Thus, the total of 2.2×10^4 events obtained in Fig. 2, or about 570 events per cm^3 of irradiated tissue, becomes 4.3×10^4 to 1.3×10^5 per cm^3 in the positron camera, assuming the same dose and tissue absorption. Decreasing the separation between detectors can further improve the sensitivity.

Two mechanisms contribute to the background. One is the presence of neutrons which may have a different distribution from the photon beam yet generate similar positron emission activity. Another process is the biological transport of activity from the generation site. The ^{15}O will be present to some extent in the molecular form $H_2\,^{15}O$, the carbon as $^{11}CO_2$, for example, which may not be retained at the irradiation site. As a result the observed distribution of activity will differ from the beam distribution.

Neutron-induced activity may be expected to be small since the threshold for the (n, $2n$) reaction in

1981, *British Journal of Radiology*, *54*, 56–60

oxygen and carbon is 20 MeV, and the fraction of neutrons with greater energy will be very small. Experimental measurement in the photon field for accelerator energies to 32 MeV revealed neutron components contributing less than 1% of the photon fluence (Wilenzick *et al.* 1973).

The relative stability of the target elements in different tissues has been studied. In skeletal muscle in rats, about 15% of the total number of positron-emitting nuclei produced were transported from the irradiation site (Bennett *et al.*, 1978). The transport or residence time was equivalent to a half-life of about 45 seconds, a component found only in live animals. This component was small and relatively constant for the different rats studied. Similar results have been obtained for proton irradiation of brain and abdomen in dogs and swine. Only in organs where blood contents are comparable in mass to the parenchyma are large fractions of the induced activity transported from the irradiation site. Biological transport appears to be the major source of background, and can constitute a significant correction in the computation of dose distribution from the activity distribution imaged by the positron camera. Further studies are required to assess bio-transport in other regions of clinical interest.

The ability to reconstruct the distribution of dose delivered throughout the treatment volume after each therapy fraction offers a mechanism for quality control at present unavailable in radiation therapy.

REFERENCES

BENNETT, G. W., ARCHAMBEAU, J. O., ARCHAMBEAU, B. E., MELTZER, J. I. and WINGATE, C. L., 1978. Visualization and transport of positron emission from proton activities *in vivo*. *Science*, *200*, 1151–1152.

COOK, B. C., BAZLIN, J. E., BRADFORD, J. N. and GRIFFIN, J. E., 1966a. $^{16}O(\gamma, n)^{15}O$ cross section from threshold to 65 MeV. *Physical Review*, *143*, 712–723.

1966b. $^{12}C(\gamma, n)^{11}C$ cross section to 65 MeV. *Physical Review*, *143*, 724–729.

JOYET, G. D., 1965. Radioactivity induced in the tissues by betatron irradiation. In *The Brown Boveri Betatron, Five Years of Research and Experience with the 31 MeV Betatron*. (Brown Boveri Corp., Switzerland, 2512 E-X11, 2 (6,56) L 2044).

MAYNEORD, M. V., MARTIN, J. H. and LAYNE, D. A., 1949. Production of radioactivity in animal tissue by high energy X-rays. *Nature*, *164*, 728–730.

SNYDER, W. S., COOK, M. J., NASSET, E. S., KARHAUSEN, L. R., HOWELLS, G. P. and TIPTON, I. H., 1975. Report of the task group on reference man. ICRP publication 23. (Pergamon Press, New York).

WILENZICK, R. M., ALMOND, P. R., OLIVER, G. D. and DEALMEIDA, C. E., 1973. Measurement of fast neutrons produced by high energy X-ray beams of medical electron accelerators. *Physics in Medicine and Biology*, *18*, 396–408.

In vivo dosimetry in the pelvis during fast neutron therapy

By B. J. Mijnheer, Ph.D., Tj. Wieberdink, M.Sc. and J. J. Battermann, M.D.

Radiotherapy Department, Antoni van Leeuwenhoek Hospital, The Netherlands Cancer Institute, Amsterdam, The Netherlands

(Received May 1980 and in revised form July 1980)

The assessment of dose distributions in patients during treatment with fast neutrons is based on measurements in a phantom material, *i.e.* water or another type of tissue equivalent (TE) liquid. Only limited information is available on fast neutron dosimetry *in vivo* in order to check how well these phantom materials simulate the average density and composition of the human body in the irradiated area. At Hammersmith Hospital, *in-vivo* dosimetry has been applied to check the dose in the oesophagus as well as the exit dose during irradiation of carcinoma of the bronchus (Field, 1971). Activation of small pellets of aluminium and measurement of the induced ^{27}Mg activity was the technique used. More recently the application of $CaSO_4$: Tm phosphor TLD (Blum *et al.*, 1976) and the activation of indium (Catterall and Bewley, 1979) have been described for dosimetry during neutron therapy in that institute. Smith *et al.* (1976) inserted silicon diodes into the oesophagus to measure the effect of intervening lung tissue on the tumour dose during therapy with the TAMVEC fast neutron beam. Treatment control by means of activation of aluminium foils placed on the skin of the patient is carried out routinely during neutron treatment in Hamburg (Franke *et al.*, 1978).

No data are available in the literature on *in-vivo* neutron dosimetry during irradiation of tumours in the pelvic region. Before starting clinical trials on pelvic tumours with the Amsterdam d+T fast-neutron therapy machine, a pilot study was undertaken (Battermann and Breur, 1979). In 20 patients in this study, the neutron dose in the rectum, and in some patients in the bladder, was measured *in vivo* to check the results determined from measurements in a water phantom.

The technique used was based on the production of ^{24}Na and ^{56}Mn in small aluminium and iron pellets respectively. The activity induced during treatment of the patient was compared with the activity measured after irradiation in a water phantom at the same depth. Counting ^{24}Na instead of ^{27}Mg in irradiated aluminium is more accurate at the lower dose rate of the d+T machine compared with the cyclotron. The activation of indium is not a suitable method for a d+T beam due to the strong variation in response with position in the beam (Ing and Cross, 1975). The counting of induced radioactivity is simple and has a higher accuracy than the use of silicon diodes, unless special precautions are taken (Prichard *et al.*, 1973). The $CaSO_4$ TLD method has a larger uncertainty than measurement of radioactivity, probably owing to the strong variation in response with neutron energy. In contrast to activation measurements, it has, however, the ability to measure the partial doses of both fast neutrons and γ rays.

It should be stressed that our *in-vivo* dosimetry technique is not absolute, *i.e.* a method to check the numerical value of the applied neutron absorbed dose. It only gives information on the neutron absorbed dose in a patient relative to that in a water phantom irradiated under the same conditions. Some preliminary results of measurements on 12 patients have already been given elsewhere (Mijnheer *et al.*, 1978).

MATERIALS AND METHODS

The Amsterdam fast neutron therapy machine consists of a shielded sealed-off d+T neutron tube emitting neutrons with a primary energy of about 14 MeV. Details of the machine and the procedures applied for clinical neutron dosimetry can be found elsewhere (Mijnheer *et al.*, 1978).

Two pellets, one of high-purity aluminium and one of iron, both 4 mm diameter and 9 mm long, were positioned just behind each other in a polyethylene catheter and brought into the rectum or the bladder. By means of AP radiographs the pellets were positioned in the middle of the treatment field. When this was not possible a correction factor was applied (see below). After fixing the catheter in the desired position by taping it carefully to the skin of the patient, a lateral radiograph was taken to determine the actual depth of the centre of the pellets under the skin. The patient was then very carefully moved from the simulator table to the treatment table in order to maintain the same position of the dosimeters during simulation and treatment. Second aluminium and iron pellets were placed on the skin at the centre of the irradiated area.

After irradiation with one field the catheter was removed from the patient and the induced radioactivity counted in the well of a 7.5 × 7.5 cm NaI (Tl) crystal which was coupled to an automatic sample changer (Philips type PW 4520). Use was made of the reactions ^{56}Fe (n,p) ^{56}Mn and ^{27}Al (n,α) ^{24}Na. ^{56}Mn has a half-life of 2.578 h and its main γ rays have energies of 847, 1810 and 2113 keV. ^{24}Na decays with a half-life of 15.03 h and has main γ energies of 1369 and 2754 keV. All pulses above a threshold of 175 keV were counted. Counting periods of 40 minutes for the aluminium pellets and 10 minutes for the iron pellets were used yielding at least 10^4 counts. The radiochemical purity was checked by measuring the half-life and the γ-ray spectrum, showing that no other activity was counted if a waiting period of two hours for the aluminium pellets was taken into account, allowing the ^{24}Mg, with a half-life of about ten minutes, to decay. The presence of any long living ^{54}Mn in iron pellets that were irradiated several times could not be detected, but would be included in the background measured before the irradiation.

The measurements in the water phantom were performed by irradiating aluminium and iron pellets positioned along the central axis of the field inside a water-filled open-top Perspex cube with outside dimensions of 30 cm and walls 0.6 cm thick. The dose gradient in the region of interest amounted to about 0.8%/mm. The irradiated field was 13 × 16 cm at 80 cm SSD. The pellets were usually exposed to a neutron absorbed dose of about 40 cGy ,which took about ten minutes.

Analysis of the measurements

The activity, A, at the end of an irradiation time, t, of a material with N atoms available for activation, can be given by:

$$A = N\phi\sigma\,(1-e^{-\lambda t}) \quad . \; . \; . \; (1)$$

where ϕ is the fluence rate of the bombarding particles, which is assumed to be constant during the irradiation, σ is the cross-section for the activation reaction and λ is the decay-constant of the radioactive material.

Activation resulting from different irradiation times with the same fluence, Φ, of particles, and thus the same number of monitor units, can be taken into account by assuming that ϕ is identical to Φ/t. The observed activity was corrected for background and decay after the end of the irradiation and normalized to the same weight which is proportional to N.

Under conditions of charged particle equilibrium the neutron absorbed dose, D_N, is almost equal to the neutron kerma, K_N. Kerma is identical to Φk, where k is the kerma factor which has been calculated for different neutron energies and materials (Caswell *et al.*, 1980). The ratio of the measured activity, corrected for different irradiation times, background and decay, to the neutron absorbed dose can now be given by:

$$\frac{At/(1-e^{-\lambda t})}{D_N}=\frac{N\Phi\sigma}{\Phi K}=N\sigma/K \quad . \quad . \quad (2)$$

If neutrons at the position of the activated materials are not mono-energetic, average values $\bar{\sigma}$ and $\bar{k}$ for the actual neutron energy spectrum at that position should be used. Changes in the fast neutron spectrum will affect the level of induced activity per unit of neutron absorbed dose. This ratio has therefore been determined along the central axis of the field in the water phantom. After normalizing the data at the surface, the ratio for iron decreases to a value of 0.9 at 4 cm deep and becomes constant at 0.86 for depths greater than 10 cm. For aluminium a similar trend could be observed. Because the ratio of the corrected activity to the neutron dose varies with depth, a calibration of the dosimeters at one depth would introduce an error. It was therefore decided to compare the corrected value of the activity produced in the pellets with that irradiated at the same depth in the patient.

The spectrum also changes from the centre towards the edges of the field, resulting in changes of several per cent in the ratio of the activity to the neutron dose over the field area and much larger changes in the penumbra. These measurements, performed at a depth of about 10 cm in the phantom, in combination with the AP radiograph, were used to determine a correction factor if the pellets were not positioned at the centre of the field.

RESULTS AND DISCUSSION

Measurements have been performed on 20 patients treated with the d+T neutron beam. A summary of the ratio of the activity measured on the patient to that in the water phantom is presented in Fig. 1 in histogram form. The mean ratio at the entrance of the beam amounts to 0.988 for the iron pellets and 0.999 for the aluminium pellets, both

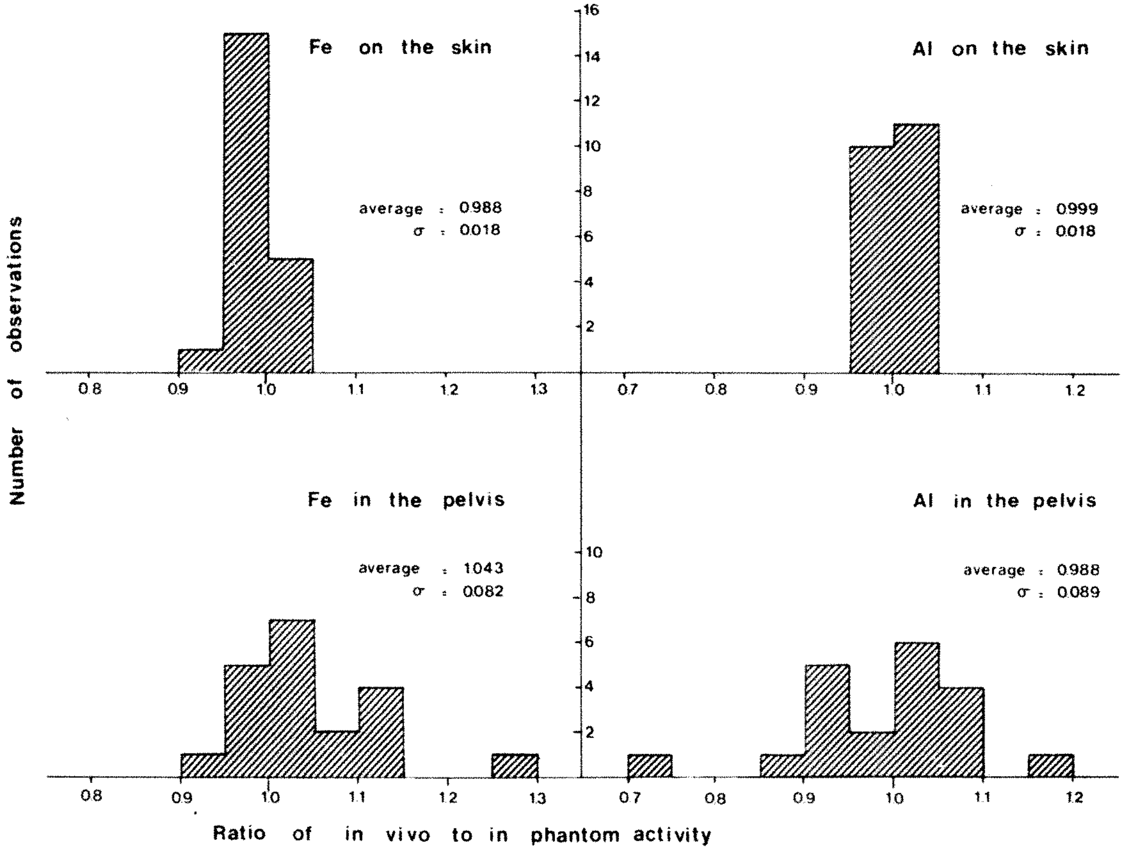


FIG. 1.

Histograms of the ratio of the activity measured on the patient to that in the water phantom at the same depth.

with a standard deviation of 0.018. This indicates that the treatments were carried out correctly. The data in the pelvis show a larger spread. Here the observed mean ratio is 1.043±0.082 for the iron pellets and 0.988±0.089 for the aluminium pellets. Within the experimental uncertainty (one standard deviation) the mean results for both the iron and the aluminium activation do not deviate from unity.

The random errors in the determination of the ratio of *in-vivo* to in-phantom activity may be due to:

(1) Uncertainty in determination from the radiograph of the depth of the pellets under the skin: 2 mm, resulting in an uncertainty of 1.7% in the activity.
(2) Uncertainty in the enlargement factor of the radiograph, from which the depth in the patient is determined: 1.0%
(3) Uncertainty in the actual position of the pellets during irradiation compared with that during simulation, due to breathing or other movements of the patient. As a result the distance from the target to the skin may differ from the value given by the treatment plan, or the depth of the pellets under the skin may be different from that on the radiograph. An estimate of both effects yielded a displacement of 8 mm, resulting in an uncertainty of 2.0% for the pellets on the skin and 7.0% in the pelvis.
(4) Uncertainty in the correction factor for spectral changes if the pellets are not on the central axis of the field: 1.0%.
(5) Uncertainty in the ratio of the activity measurements: 0.8% at the surface and 1.5% at depth.

The estimated total uncertainty amounts to 2.2% for the measurements on the skin, which agrees well with the observed value of 1.8%. The measurements in the pelvis have somewhat larger standard deviations, 7.9% and 9.0%, compared with the estimated total uncertainty of 7.5%.

Three other sources of uncertainty, which are difficult to quantify, may enhance the estimated error:

(a) The presence of gas in the gut, which could be observed from some of the radiographs, may cause a change in the neutron fluence at the position of the pellets compared with the situation without gas.
(b) The average composition and density of the treated area in the patient is not identical to water.
(c) During transport of the patient from the simulator room to the treatment room the position of the pellets may change.

(a) The influence of the first effect was estimated from measurements on pellets placed at the backside of an air-filled Perspex tube with an internal diameter of 32 mm. An increase of about 17% for both the aluminium and iron activation was observed. This indicates that gas volumes would have a large influence on the observed activity, resulting in an average ratio of *in-vivo* to in-phantom activity larger than one for ^{24}Na as well as ^{56}Mn. Because the mean ratios are not far from unity, the influence of gas volumes on the *in-vivo* measurements must be compensated by the composition and density of soft tissue, bone and other materials in the pelvis.

(b) The composition and density of water are not identical to those of soft tissue. A muscle-equivalent liquid with a density of 1.07 g cm^{-3} and a composition identical to ICRU muscle tissue (Frigerio *et al.*, 1972) might be a better phantom material to simulate human tissue in the pelvic region. The *in-vivo* dosimetry measurements were therefore also compared with activation measurements at the same depth in the Perspex cube filled with such a TE liquid. An analysis of the ratio of the *in-vivo* activities to those in phantom for the TE liquid gave a mean value 0.5% lower for the Al and Fe measurements at the skin, and 1.7% higher in the pelvis. The standard deviation of the analysis relative to water or to TE liquid was about the same, indicating that the use of TE liquid instead of water does not give a better agreement with the *in-vivo* dosimetry results.

(c) Movement of the pellets in the patient after the lateral radiograph was taken may result in a change in depth of the pellets under the skin. The effect of movement of the pellets on the observed activity ratio will depend on the direction of the catheter at the position of the pellets with respect to the skin surface. It was observed that this direction varied strongly between different patients, mainly due to the presence of tumour. No relationship could be observed between the slope of the catheter with respect to the skin and the deviation of the activity ratio from the mean value.

CONCLUSIONS

As pointed out already by Field (1971), the activation method for *in-vivo* fast neutron dosimetry has the advantages that the detectors can be small, the technique is easy to perform, sensitive, accurate and insensitive to γ rays. Because the irradiation time is much shorter than the half-lives of the nuclides produced (^{24}Na and ^{56}Fe), the calibration hardly depends on the irradiation time or on the distribution of neutron fluence rate during this period. The results of *in-vivo* measurements at the skin and in the pelvis of 20 patients show that within the experimental uncertainty the activity produced in aluminium and iron pellets was equal to that induced in the pellets at the same depth in a water phantom. The agreement was not improved if the *in-vivo* data were compared with activation measurements in a TE liquid. It can be concluded that water is a good phantom material to simulate the average density and composition of the pelvic region of the human body during fast neutron therapy.

ACKNOWLEDGMENT

We wish to thank Peter Visser for stimulating discussions and help with some of the measurements.

REFERENCES

BATTERMAN, J. J. and BREUR, K., 1979. Results of fast neutron radiotherapy at Amsterdam. In: *Proceedings of the Third Meeting on Fundamental and Practical Aspects of the Application of Fast Neutrons and Other High LET Particles in Clinical Radiotherapy*, Supplement to *European Journal of Cancer*, 17–22.

BLUM, E., HEATHER, J. D., BEAL, A. D. R. and BEWLEY, D. K., 1976. Calcium sulphate phosphor for clinical neutron dosimetry. *Health Physics*, *30*, 257–261.

CASWELL, R. S., COYNE, J. J. and RANDOLPH, M. L., 1980. Kerma factors for neutron energies below 30 MeV. Submitted to *Radiation Research*.

CATTERALL, M. and BEWLEY, D. K., 1979. *Fast neutrons in the treatment of cancer* (Academic Press, London).

FIELD, S. B., 1971. An *in vivo* dosimeter for fast neutrons. *British Journal of Radiology*, *44*, 891–892.

FRANKE, H. D., HESS, A., MAGIERA, E. and SCHMIDT, R., 1978. The neutron therapy facility (DT, 14 MeV) at the Radiotherapy Department of the University Hospital Hamburg-Eppendorf. *Strahlentherapie*, *154*, 225–232.

FRIGERIO, N. A., COLEY, R. F. and SAMPSON, M. J., 1972. Depth dose determinations I. Tissue-equivalent liquids for standard man and muscle. *Physics in Medicine and Biology*, *17*, 792.

ING, H. and CROSS, W. G., 1975. Spectra and dosimetry related to neutron irradiations of the human body. *Physics in Medicine and Biology*, *20*, 906.

MIJNHEER, B. J., VISSER, P. A. and WIEBERDINK, TJ., 1978. Clinical neutron dosimetry at the Amsterdam fast neutron therapy facility. In: *Proceedings Third Symposium on Neutron Dosimetry in Biology and Medicine*, EUR 5848, 203–225. (Commission of the European Communities, Luxembourg).

PRICHARD, N. M., SMITH, A. R. and ALMOND, P. R., 1973. Silicon diodes as dosimeters in fast neutron therapy. *American Association of Physicists in Medicine Quarterly Bulletin*, *7*, 92.

SMITH, A. R., JARDINE, J. H., RAULSON, G. L., ALMOND, P. R. and BOYD, D. D., 1976. *In vivo* measurements of lung corrections for fast-neutron therapy. *Medical Physics*, *3*, 391–396.

Book review

Treatment of Radioresistant Cancers. Edited by M. Abe, K. Sakamoto and T. L. Phillips, pp. viii+230, 1979 (Elsevier/North Holland Biomedical Press, Amsterdam), DM.95.00/$46.25.

ISBN 0-444-80179-0

This little book has a slightly misleading title; it is the proceedings of an international symposium on the "Prospects for treatment of radio-resistant cancers" held in Kyoto (Japan) on May 21, 1979. The symposium dealt almost entirely with newer methods aimed at increasing the therapeutic ratio of radiotherapy and thereby improving local control rates of tumours which are sometimes radio-curable but where radiotherapy often fails.

There are three main sections dealing with hypoxic-cell sensitizers, hyperthermia, and high LET radiation, with a final miscellaneous section containing contributions on the results of radiotherapy for soft-tissue sarcoma, uneven fractionation in radiotherapy of lung cancer, combined treatment with bleomycin and radiation, and the vasculature of experimental tumours. In each of the first three sections there are excellent summaries of the experimental basis of the techniques under discussion. The current clinical experience with both misonidazole and hyperthermia are well summarized. There are accounts of small series of patients treated in Japan by californium brachytherapy and a 30 MV neutron beam, and in Los Alamos with pions. In all instances the conclusion seems to be that the method under study shows promise but its effectiveness remains to be proved.

To this reader the most fascinating aspect was the fact that the theoretical basis for most of these new approaches depends partly or wholly on the oxygen effect, yet the one technique which shows the greatest enhancement in experimental tumour systems, and which has been demonstrated by controlled clinical trials to improve both therapeutic ratio and survival in at least one type of human cancer, gets only one passing mention in the entire book. This is in the introduction to one paper where the authors state that "hyperbaric oxygen has been demonstrated to be unsatisfactory"; if this indeed be so, one is left wondering what is the likely fate of the methods of treatment discussed in this volume!

This book provides a quite useful and reasonably up-to-date summary of the current status of many of the laboratory and clinical studies of hypoxic cell sensitizers, hyperthermia and high LET radiation. It should be read by any radiotherapist who is interested to know what is going on in these fields in North America and Japan, but no doubt many of the contributions will soon be out of date as these studies progress.

J. M. HENK.

1981, *British Journal of Radiology*, 54, 61–65 JANUARY 1981

Case reports

Achondrogenesis type II in twins

By P. E. Andersen, Jr., M.D.

Department of Diagnostic Radiology, University Hospital, DK-5000 Odense C, Denmark

(*Received June 1980 and in revised form August 1980*)

Achondrogenesis is a congenital skeletal dysplasia, which is characterized clinically by a large head, short trunk with distended abdomen and underdeveloped skeleton with short extremities. The condition is a rare autosomal recessive hereditary disease and is incompatible with life.

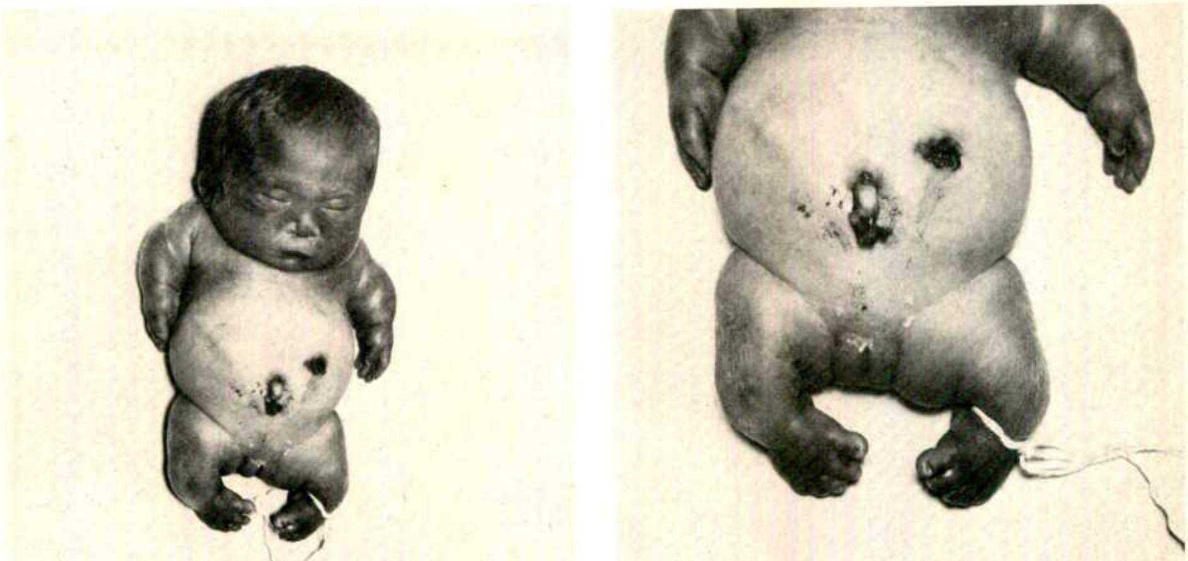
CASE REPORT

The infants were monochoriotic, diamniotic twin girls born to a 30-year-old gravida 2 para 2. The first-born child was without congenital abnormality. The mother had not taken any teratogenic compounds during the pregnancy in question. There was no known bone disease or growth defects in any of the families of the parents, both of which were very large, and the parents were not related.

The twins were approximately ten weeks premature (twin A, weight 920 g, length 24 cm; twin B, weight 1090 g, length 24 cm), moribund at birth and died after 90 min. They both had similar appearance (Fig. 1A, B). The head was large, wide and square with a flat nose, and the tongue was split at the tip. The neck was short, the chest narrow and short, and the lungs were hypoplastic (at autopsy). The trunk was short and broad with a prominent abdomen, a wide epigastric angle and the liver palpable 2–3 cm below the costal margin. The extremities were short and thick with almost rudimentary lower legs and arms. Both the hands and feet were small and wide, but well formed without abnormal grooving.

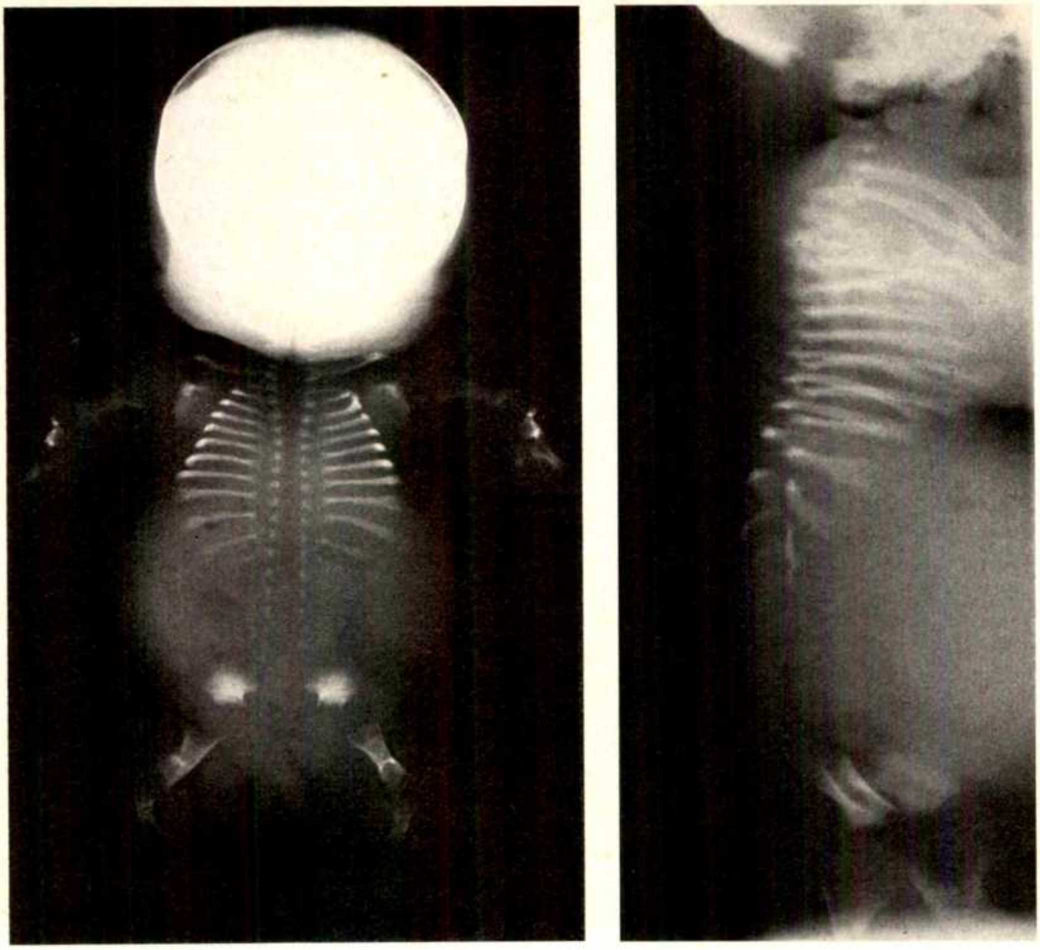
Histological examination revealed changes in the epiphyseal cartilage with severely abnormal resting cartilage, inasmuch as the cartilaginous cells were enlarged with a reduction in the cartilaginous matrix, in intercellular substance and with invasive connective tissue and blood vessels. There was no actual proliferation zone and no regular column arrangement of the proliferating cartilaginous cells down towards the ossification zone, where the cartilaginous cells were ballooned and degenerate. The ossification zone itself in the epiphyseal disc was very irregular with a few diversely orientated primary trabeculae, but apparently with normal osteoid formation and calcification of the bone.

Radiologically (Figs. 2A, B, 3 and 4), the long bones were considerably shortened, of reduced density and with flaring of the ends, further, the legs (below knee) and forearms were curved. No ossification nuclei could be seen in the carpal or metacarpal bones, nor were the distal femoral nuclei present. In the pelvis, definite ossification could be seen only in the ilia, with no nuclei visible in the ischium, pubis or sacrum. Very faint shadows of the vertebral bodies could be observed in the upper lumbar region only, whereas development of the neural arches could be seen throughout the vertebral column. The costal elements were short, but otherwise normal. Ossification was not present in the sternum but



A FIG. 1. B

Twin A. Premature infant with achondrogenesis. Characteristic features are: short trunk with distended abdomen, large head and micromelia.



A FIG. 2 B

Radiographs of same infant in anterior and lateral projections. Marked micromelia and lack of ossification of the axial skeleton are prominent features.

TABLE I

ACHONDROGENESIS

	Type I Fraccaro-Houston-Harris type	Type II Langer-Saldino type
Skull	Poor ossification of calvarium	Normal ossification of calvarium; calvarium relatively larger than in type I
Thorax	Thin ribs with flared anterior ends. Usually multiple rib fractures	Ribs short and stubby. Absence of rib fractures
Spine	Absent or small ossified centres of vertebral bodies; posterior elements present	Absent or extremely retarded vertebral bodies, especially in lumbar region
Pelvis	Poorly ossified iliac bones; sacrum and pubic bones absent	Iliac bones small but relatively well ossified; deficient sacrum and pubic bones
Limbs	Short and broad bones, often with marked bowing of shafts. Flared metaphyses with spurs	Changes less gross; short, better shaped tubular bones with cupping and flaring of metaphyseal ends and usually diaphyseal constriction
Histology	Severe retardation of chondrocytic proliferation in physeal cartilage. Abundant cartilage matrix	Large chondrocytes. Degeneration of the chondrocytes, especially in the physeal growth region. Less cartilage matrix

Both types are lethal, micromelic types of dwarfism with relatively large head in relation to the trunk.

TABLE II

DIFFERENTIAL DIAGNOSIS OF SHORT-LIMBED DWARFISM

	Achondrogenesis	Thanatophoric dwarfism	Asphyxiating thoracic dystrophy	Hypophosphatasia	Achondroplasia ("chondrodystrophy")
History	Fatal at birth	Fatal at birth	Usually fatal at birth	In severe cases fatal at birth	Homozygous may be fatal at birth; heterozygous compatible with life
Genetics	Autosomal recessive	Unknown	Autosomal recessive	Autosomal recessive	Autosomal dominant
Clinical appearance	Relatively large head; narrow thoracic cage; short trunk with distended abdomen—hydrops fetalis; micromelia	Disproportionate large head with low-lying nasal bridge; more narrow thoracic cage; normal trunk length with distended abdomen; micromelia	Normal cranial vault; very narrow thoracic cage; mesomelic micromelia, short hands and feet, polydactyly possible	Caput membranaceum; narrow thoracic cage; the child with a larger trunk and length featuring more finely modelled long bones (pseudo)-micromelia	Protruding forehead; depressed, flattened nasal bridge; chest wall developed; comparatively long trunk; rhizomelial micromelia (especially upper arms); legs bowed; trident hand
Radiology skull	Enlarged with poor or normal ossification; normal base	Enlarged with mild frontal bossing; short base; narrow foramen magnum; well ossified bones	Normal cranial vault	Poorly ossified vault (caput membranaceum), almost devoid of bone, but small areas of ossification within the facial bones and mandible	Enlarged with normal ossification; short base; narrow foramen magnum
thorax	Short horizontal ribs, possibly with fractures; absent sternal ossification	Very short horizontal ribs; sternal ossification may be delayed	Very short thick ribs, expanded anteriorly	The ribs short but slender and poorly mineralized; clavicles narrow and curved, relatively short	The ribs a little short and flared, but costal cartilages long; clavicles normal
spine	Vetebral bodies barely perceptible; failure of ossification especially in cervical and lumbar spine; normal interpedicular space; moderate increase in height of disc space; sacrum not ossified	Vertebral bodies present with flattened and deformed outline; interpedicular space reduced; increase in height of disc space; sacrum present	Vertebral bodies normal, with normal height; normal interpedicular distance	Ossification centres in thoraco-lumbar region, but not in any other vertebral bodies; interpedicular distance is not seen	Characteristically shaped and slightly flattened vertebral bodies; narrower interpedicular distances in lumbar region; sacrum narrow and short
pelvis	Iliac bones short, wide, poorly ossified, with flat, concave acetabular angle; no narrowing of the sacrosciatic notch; ischial and pubic bones absent or extremely delayed ossification	Iliac bones short, wide; flat acetabular roof, and narrow sacrosciatic notch; ischial and pubic bones short and thick without delayed ossification; sacrum ossified	Iliac bones square with a shallow sacrosciatic notch; flat acetabular angle	Irregular, poorly ossified ilium; acetabular angle not seen; narrow sacrosciatic notch	Iliac bones squared, small, wide; flat acetabular angle; narrow sacrosciatic notch; ischium and pubic bones of nearly normal size; the sacrum articulates low between the iliac wings

TABLE II (*continued*)

DIFFERENTIAL DIAGNOSIS OF SHORT-LIMBED DWARFISM

	Achondrogenesis	Thanatophoric dwarfism	Asphyxiating thoracic dystrophy	Hypophosphatasia	Achondroplasia ("chondrodystrophy")
Radiology extremities	Very short wide shafts and flared, cupped ends; periosteal spurs may be present; femora not bowed	Very short with bowed shafts of normal width; femora bowed and deformed and bony thorn-like projections of proximal femora	Moderately short extremities; the ends of the metaphyses slightly frayed and irregular; precocious ossification centres present at the proximal ends of humerus and femur, but no ossification centres at the knee	Short distorted limbs with thin, poorly ossified shafts of the long bones; minute areas of ossification at the upper ends of humerus, femur and tibia	Slightly bowed, short shafts with expanded metaphyses; femora and femoral necks very short

there was normal development of the clavicles. The head appeared large but with normal ossification. There were no visible lung or heart shadows, and no abdominal air.

DISCUSSION

Due to its rarity, achondrogenesis is still a relatively unknown and poorly understood disease entity. It has been classified into types I and II, the difference being radiological and presumably merely a difference in degree. Both types are lethal, but bone dysplasia of the extremities is most pronounced in type I (Table I).

Schulte *et al.* (1978) traced a total of 54 cases of achondrogenesis in the literature and added a further two cases of their own.

The differential diagnosis is mostly between thanatophoric dwarfism, asphyxiating dystrophy, hypophospatasia and achondroplasia (Table II). The radiological differentiation is not difficult, as the pronounced retardation of skeletal ossification in cases of achondrogenesis is pathognomonic. Thus the ossification of vertebral bodies, sacrum, pubis,

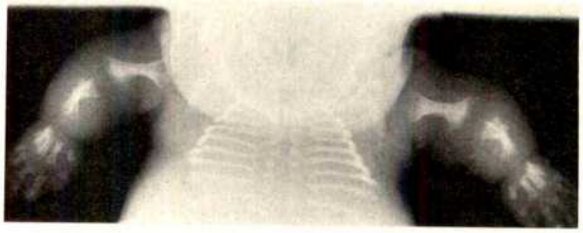


FIG. 3.

Close-up of upper extremities. Marked shortening and bowing of the forearm bones with flaring and cupping of the metaphyses.

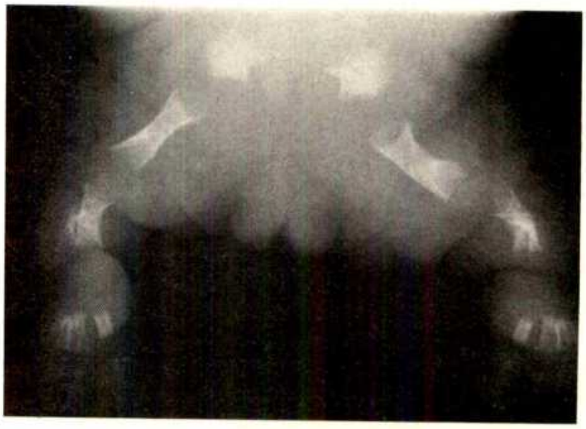


FIG. 4.

Close-up of lower extremities and pelvis. Absent ossification of sacral, ischial and pubic bones. Micromelia with metaphyseal flaring, cupping and bowing of the tibia and fibula. No tarsal bones ossified.

calcaneum and talus is not visible in the second trimester, as is the case with the normal fetus. In addition, the long bones are short, generally without any particular bowing and with irregular metaphyseal borders. The thanatophoric dwarf has clearly-visible bowing of the long bones and radiologically visible vertebral bodies, sacrum, pubis as well as the ischium, and a relatively normal length of trunk. In asphyxiating thoracic dystrophy premature centres are seen in humerus and femur, and in hypophosphatasia there is "caput membranaceum" and deformed extremities due to bone softening together with a larger trunk. The achondroplastic patient has less abnormality of the long bones; mental development is normal and the condition compatible with life.

Many of the cases of achondrogenesis described to date have occurred familially (Anteby *et al.*, 1977; Houston *et al.*, 1972; Saldino, 1971; Schulte *et al.*, 1978). Achondrogenesis is an autosomal recessive (Curran *et al.*, 1974; Houston *et al.*, 1972; Saldino, 1971; Schulte *et al.*, 1978) whereas achondroplasia is an autosomal dominant and compatible with life. A correct diagnosis is therefore of importance with regard to genetic counselling. Many cases of achondrogenesis and thanatophoric dwarfism are mistaken for achondroplasia and, with a negative family history, regarded as dominant mutations. Parents may thus be given an encouraging prognosis for future offspring even though there is a 25% risk of subsequent children being born with the same defect.

Prenatal diagnosis is possible, and ultrasound examination and plain radiography of the abdomen should be advised in cases of future pregnancies. It has been possible to make the diagnosis prenatally on plain radiography, in a few cases, as early as in the 22nd to 24th weeks of gestation (Anteby *et al.*, 1977; Curran *et al.*, 1974; Houston *et al.*, 1972; Saldino, 1971). In a single case the diagnosis was made in the 20th week of pregnancy by means of amniography (Golbus *et al.*, 1977).

REFERENCES

ANTEBY, S. O., AVIAD, I. and WEINSTEIN, D., 1977. Prenatal diagnosis of achondrogenesis. *Radiologia clinica*, *46*, 109–114.

CURRAN, J. P., SIGMON, B. A. and OPITZ, J. M., 1974. Lethal forms of chondrodysplastic dwarfism. *Pediatrics*, *53*, 76–85.

GOLBUS, M. S., HALL, B. D., FILLY, R. A. and POSKANZER, L. B., 1977. Prenatal diagnosis of achondrogenesis. *The Journal of Pediatrics*, *91*, 464–466.

HOUSTON, C. S., AWEN, C. F. and KENT, H. P., 1972. Fatal neonatal dwarfism. *Journal of the Canadian Association of Radiologists*, *23*, 45–61.

SALDINO, R. M., 1971. Lethal short-limbed dwarfism: achondrogenesis and thanatophoric dwarfism. *American Journal of Roentgenology*, *112*, 185–197.

SCHULTE, M. J., LENZ, W. and VOGEL, M., 1978. Letale Achondrogenesis: eine Übersicht über 56 Fälle. *Klinische Pädiatrie*, *191*, 327–340.

Pulmonary opacities in pseudoxanthoma elasticum: report of two cases

By H. Mamtora, M.B., Ch.B., D.M.R.D., F.R.C.R.
Department of Diagnostic Radiology, University of Manchester
and V. Cope, M.B., B.Chir., D.M.R.D., F.R.C.R.
Manchester Royal Infirmary, Oxford Road, Manchester

(Received July 1980 and in revised form August 1980)

Pseudoxanthoma elasticum (PXE) is an uncommon hereditary connective tissue disorder characterized by involvement of skin, blood vessels and the eyes.

Pathologically, there is degeneration and fragmentation of elastic tissue, often accompanied by calcification. In the skin, these changes may lead to loss of elasticity and development of yellowish papules, particularly over the neck, axillae and groins. In the eye, rupture of elastic fibres in the choroid leads to formation of angioid streaks; impairment of visual acuity may result from retinal haemorrhages and choroido-retinal degeneration. Vascular changes may lead to the development of peripheral vascular disease, hypertension and cerebral vascular disease. Skeletal abnormalities have been described and are presumed to be due to involvement of nutrient vessels (Prick and Thijssen, 1977).

Degenerative changes in the visceral vessels may be responsible for recurrent episodes of unexplained gastrointestinal bleeding; angiomatous malformations in the liver and spleen and aneurysms have been also described (Bardsley and Koehler, 1969).

Calcification may be seen in the aorta and peripheral vessels, skin and ligamentous structures. In 1952 Wolff *et al.* reported a case of PXE in a nine-year-old boy whose chest radiograph showed fine punctate opacities in the left lung. McKusick (1972) has noted similar features in both lungs of a 32-year-old man. In both patients there was a history of severe recurrent gastrointestinal haemorrhage.

We report two further cases with similar opacities on the chest radiograph.

CASE 1

A 42-year-old woman was referred from another hospital for further management of recurrent severe gastrointestinal bleeding. She had typical skin changes of PXE in both antecubital fossae, axillae and over the abdomen. Angioid streaks were present in the left eye.

There was no relevant family history and no evidence of peripheral vascular disease. Barium studies were normal and upper GI endoscopy showed abnormal mucosa, similar to that described in PXE, with alternating yellow and red areas (prominent vessels) in the antrum. Coeliac axis angiography revealed an extensive angioma involving the spleen and proximal stomach wall, with major feeding vessels from the splenic and left gastric arteries, but the short gastric and left inferior phrenic arteries were involved as well (Fig. 1).

Prior to sub-total gastrectomy, vagotomy and splenectomy, a chest radiograph showed fine densities localized to the mid-zone in the right lung (Fig. 2).

CASE 2

A 58-year-old man was first seen in 1959 with a history of poor vision in the left eye; fundoscopy showed angioid streaks in both eyes. In 1964 he developed deteriorating vision in the right eye, and clinical examination revealed minor changes of PXE in the skin over the neck. Since 1970 he has had intermittent claudication in both legs; all lower limb pulses except the left femoral were absent. Increasing symptoms in 1973 led to arteriographic studies which showed complete occlusion of the abdominal aorta below the renal arteries. There was symptomatic relief following an aortic bifurcation graft; biopsy of the resected aorta showed only atheromatous changes but no calcification associated with elastic fibres, which generally appeared normal. In 1975 he suffered several attacks of transient cerebral ischaemia, affecting the right side, but these have not been particularly troublesome in recent years.

A chest radiograph showed punctuate densities in a localized area in both lung fields (Figs. 3A, B).

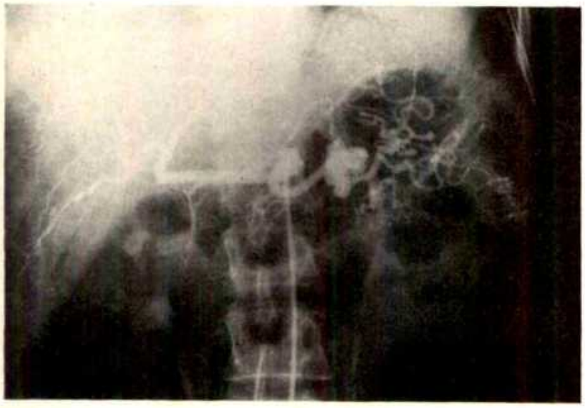


FIG. 1. *Case 1.*

Coeliac axis angiogram. Extensive angioma with major feeding vessels from splenic and left gastric arteries.

DISCUSSION

In PXE soft tissue calcification may occur in the skin, blood vessels and ligaments.

As far as we are aware, there have been only two cases reported showing pulmonary densities in PXE (Wolff *et al.*, 1952; McKusick, 1972). The origin of these is uncertain; Wolff *et al.* suggested they may be due to multiple small haemorrhages, resulting in haemosiderin deposition. Alternatively, these changes may represent calcification following degeneration and fragmentation of elastic fibres in small vessels.

Whatever the cause, we feel that the features seen on the chest radiograph are distinctive enough to suggest a diagnosis of PXE. In all cases of recurrent gastrointestinal bleeding, particularly when repeated barium studies are negative, detection of these opacities on the "routine" chest radiograph, or

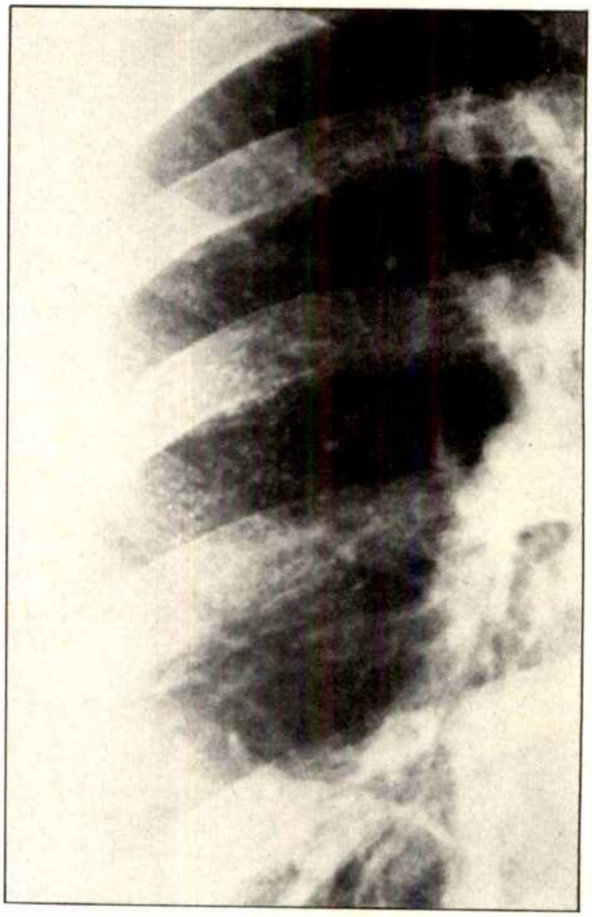


FIG. 2. *Case 1.*

Chest PA—close-up of right mid-zone.

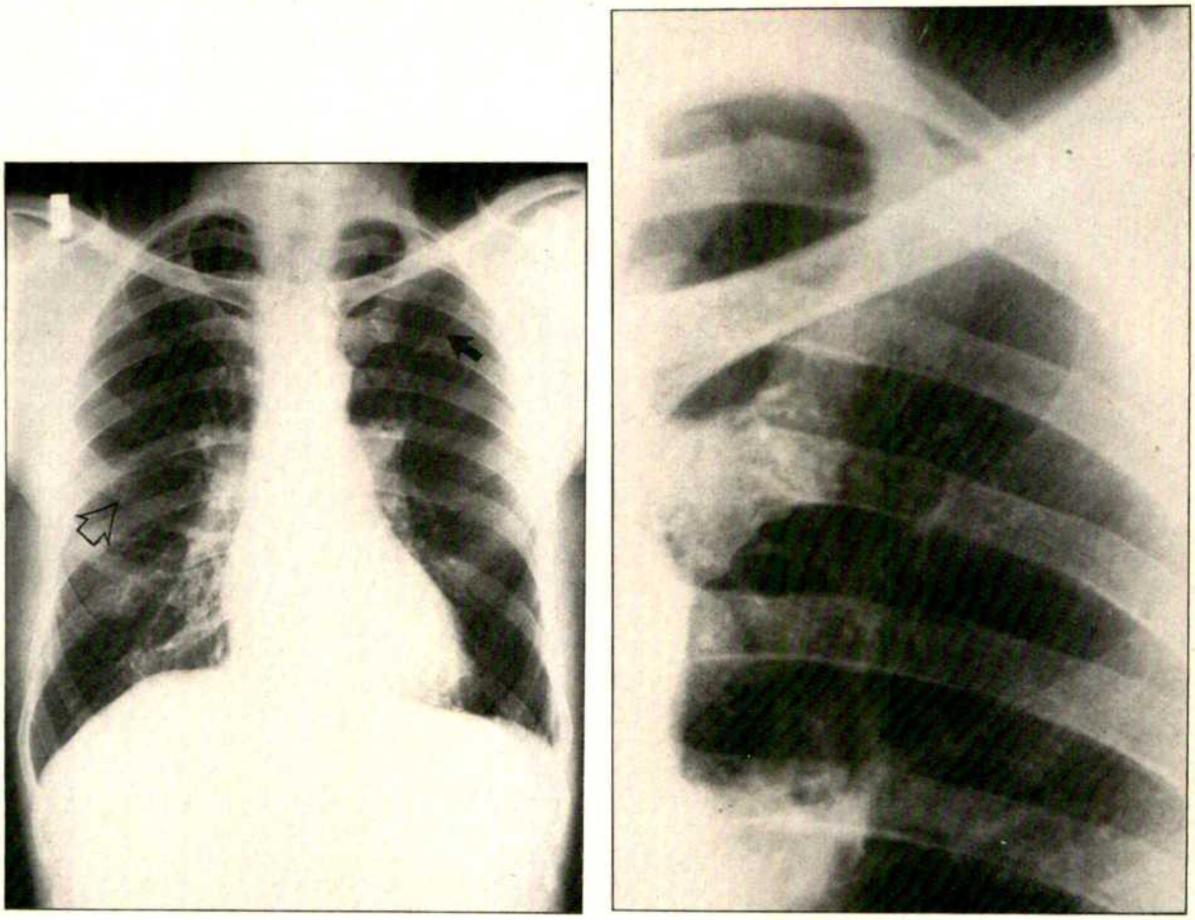


FIG. 3. *Case 2.*

(A) Chest PA—punctate densities in left upper and right mid-zones (arrows). (B) Close-up of left upper zone.

at fluoroscopy of the chest during the barium examination, may lead the radiologist to first suggest this diagnosis. Similarly, close scrutiny should be made for these abnormalities in patients with peripheral vascular disease, cerebral vascular disease and hypertension.

REFERENCES

BARDSLEY, J. L. and KOEHLER, P. R., 1969. Pseudoxanthoma elasticum: angiographic manifestations in abdominal vessels. *Radiology*, *93*, 559–562.

MCKUSICK, V. A., 1972. *Heritable Disorders of Connective Tissue*. 4th ed., p. 476 (C. V. Mosby Co., St. Louis).

PRICK, J. J. G. and THIJSSEN, H. O. M., 1977. Radiodiagnostic signs in pseudoxanthoma elasticum generalisatum (dysgenesis elastofibrillaris mineralisans). *Clinical Radiology*, *28*, 549–554.

WOLFF, H. H., STOKES, J. F. and SCHLESINGER, B. E., 1952. Vascular abnormalities associated with pseudoxanothoma elasticum. *Archives of Disease in Childhood*, *27*, 82–88.

1981, *British Journal of Radiology*, *54*, 68–69

Case reports

Chronic recurrent pleural effusion in adult histiocytosis–X

By P. W. Tittel, M.D.

Department of Radiology, Veterans Administration Medical Center, Louisville, Ky. 40202, USA

and C. F. Winkler, M.D.

Division of Hematology—Oncology, Veterans Administration Medical Center, Louisville, Ky. 40202, USA
and Department of Medicine, Trover Clinic, Madisonville, Ky., USA

(*Received June 1980*)

Histiocytosis–X is a disorder manifested pathologically by histiocytic infiltration of tissues in one or more body sites. The term "Histiocytosis–X" has been applied to a group of disorders including eosinophilic granuloma, Hand-Schüller Christian disease and Letterer-Siwe disease. Pulmonary involvement occurs as part of a generalized disease process or as a separate entity referred to as primary pulmonary histiocytosis–X.

Pleural effusion has been described as a rare manifestation of the disease in children (Matlin *et al.*, 1972; Carlson *et al.*, 1976). It is not, however, considered in the description of the disease in either the primary pulmonary or disseminated form in the adult (Weber *et al.*, 1969; Takahashi *et al.*, 1966; Pruzanski and Altman, 1964; Clark *et al.*, 1970; Nadeau *et al.*, 1960). We report a case of chronic recurrent pleural effusion in adult disseminated histiocytosis–X. To our knowledge, this is the first such case to be reported.

Case Report

A 59-year-old white male with the classic triad of exophthalmus, diabetes insipidus and bone destruction presented in March of 1978 with shortness of breath, pedal oedema and increasing proptosis of the right eye. A ^{99}Tc^{m} PYP bone scan revealed multiple areas of increased radioactivity, computerized axial tomography demonstrated bilateral retro orbital masses and chest radiograph revealed cardiomegaly and bilateral pleural effusion (Fig. 1).

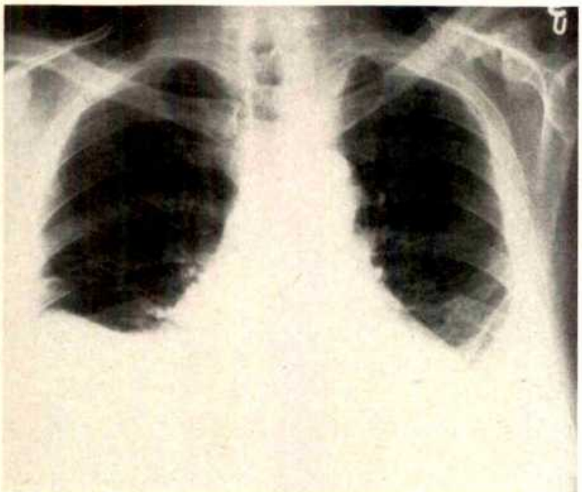
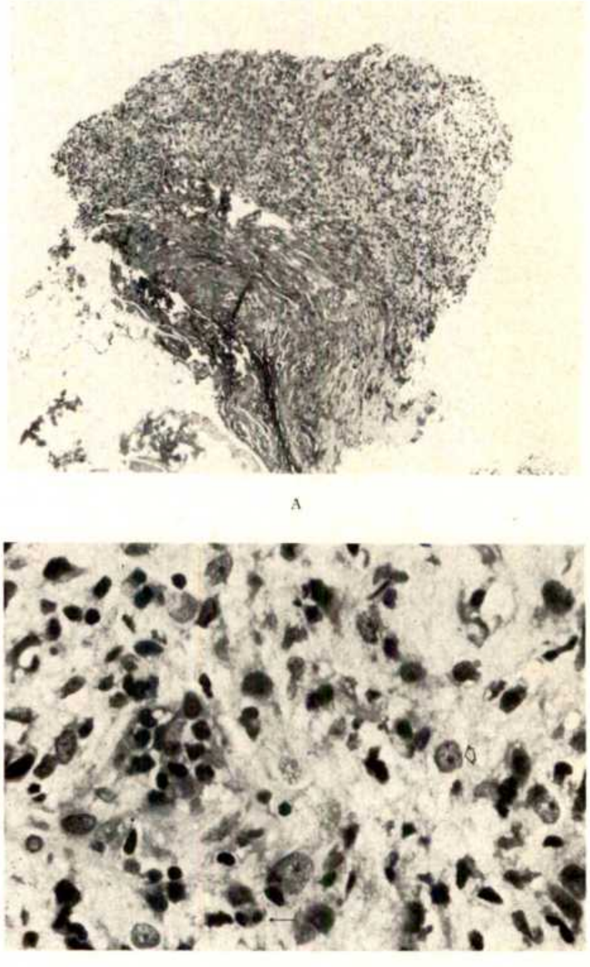


Fig. 1.

PA upright chest radiograph, March 1978. Bilateral pleural effusions and cardiomegaly.



A

B

Fig. 2.

(A) Pleural biopsy showing fibroadipose tissue and skeletal muscle underlying a large collection of histiocytes. (Hematoxylin-Eosin ×40).

(B) Pleural biopsy demonstrating abnormal collection of histiocytes (hollow arrow) and eosinophils (black arrow). (Hematoxylin-Eosin ×400).

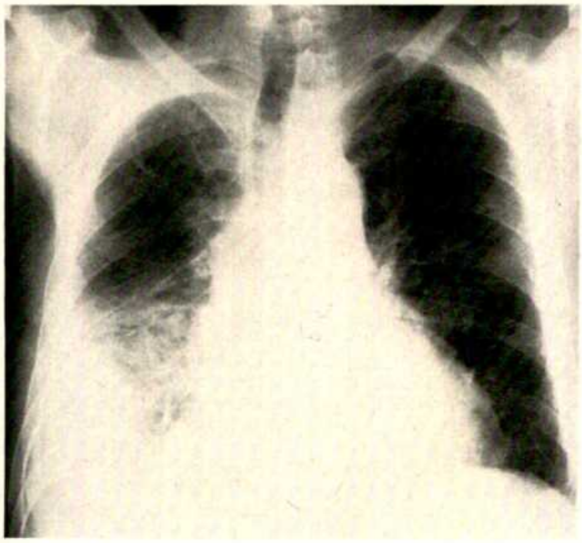


FIG. 3.

PA upright chest radiograph, April 1978. Large right pleural effusion and cardiomegaly.

Thoracocentesis was performed and the pleural fluid was compatible with an exudate. Cope needle biopsy of the pleura (Fig. 2A, B) showed fragments of muscle and fibro-adipose containing large aggregates of atypical mononuclear cells and eosinophils histologically consistent with involvement of pleural tissues by histiocytosis–X. In April 1978, because of recurrent pleural effusion necessitating repeated thoracocentesis for relief of dyspnoea and exophthalmos, cytoxic chemotherapy was begun and continued for six months. A chest radiograph at initiation of therapy (Fig. 3) revealed a diffuse coarse reticular pattern bilaterally and the presence of a right pleural effusion. Following completion of his chemotherapy, there was marked regression of the exophthalmos and reduction in his thoracocentesis requirement for symptomatic improvement of dyspnoea.

DISCUSSION

Weber *et al.* (1969) have detailed the pulmonary changes seen in histiocytosis–X. Radiographically, the disease evolves through an early alveolar exudative phase to a reticulo-nodular interstitial phase to result eventually in a fibrotic scarred lung indistinguishable from other cases of honeycomb lung, except for its apical predominance.

Spontaneous pneumothorax occurs in more than 20% of patients with histiocytosis–X. Hilar and mediastinal lymphadenopathy is rare (Fraser and Pare, 1979).

Guardia *et al.* (1979) recently reported two cases of histiocytosis–X in which pleural effusions were a prominent clinical and radiographic feature. In our case, as in those of Guardia, the diagnosis of histiocytosis–X did not appear appropriate in the light of the presence of the effusion. Instead, tuberculous pleuritis was strongly suspected as the aetiology. The pleural biopsy, however, showed histological changes typical of histiocytosis–X and the subsequent clinical course confirms the diagnosis.

The radiologist should be aware of the possibility of pleural effusion as a direct manifestation of histiocytosis–X in those cases of the disease where the effusion fails to respond to therapy directed toward more common causes of pleural effusion.

REFERENCES

CARLSON, R. A., HATTERY, R. R., O'CONNELL, E. J. and FONTANA, R. S., 1976. Pulmonary involvement by histiocytosis–X in the pediatric age group. *Mayo Clinic Proceedings*, *51*, 542.

CLARK, R. L., MARGULIES, S. I. and MULHOLLAND, J. H., 1970. Histiocytosis–X. A fatal case with unusual pulmonary manifestations. *Radiology*, *95*, 631.

FRASER, R. G. and PARE, J. A., 1979. *Diagnosis of Diseases of the Chest.* 2nd ed., Vol. III, p. 1733 (W. B. Saunders, Philadelphia)

GUARDIA, J., PEDREIRA, J. D., ESTEBAN, R., VARGA, V. and ALLENDE, E., 1979. Early pleural effusion in histiocytosis–X. *Archives of Internal Medicine*, *139*, 934–936.

MATLIN, A. H., YOUNG, L. W. and KLEMPERER, M. R., 1972. Pleural effusion in two children with histiocytosis–X. *Chest*, *61*, 33.

NADEAU, P. J., ELLIS, F. H., JR., HARRISON, E. G., JR. and FONTANA, R. S., 1960. Primary pulmonary histiocytosis–X. *Diseases of the Chest*, *37*, 325.

PRUZANSKI, W. and ALTMAN, R., 1964. Histiocytosis–X in adult with predominant pulmonary manifestation. *Archives of Internal Medicine*, *113*, 261.

TAKAHASHI, M., MARTEL, W. and OBERMAN, H. A., 1966. The variable roentgenographic appearance of idiopathic histiocytosis. *Clinical Radiology*, *17*, 48.

WEBER, W. N., MARGOLIN, F. R. and NEILSEN, S. L., 1969. Pulmonary histiocytosis–X. A review of 18 patients with reports of six cases. *American Journal of Roentgenology*, *107*, 280.

A case of non-fatal intravasation of barium during barium enema

By F. Holly Archer, M.B., B.Ch. and A. H. Freeman, M.B., F.R.C.R.

Department of Diagnostic Radiology, Addenbrooke's Hospital, Cambridge

(*Received January 1979 and in revised form July 1980*)

Venous intravasation of barium is a very rare complication of barium enemas. There are ten reported cases in the literature and only two of these have survived. The factors which have been suggested as contributory are:

(1) mucosal inflammation such as may be found in

association with ulcerative colitis or diverticulitis (Isaacs *et al.*, 1950; Karen *et al.*, 1974; Truemner *et al.*, 1960);

(2) intestinal obstruction (Karen *et al.*, 1974; Noveroske, 1970);

(3) increased intraluminal pressure by use of a balloon catheter (Truemner *et al.*, 1960; Roman *et al.*, 1952; Rosenberg and Fine, 1959);

(4) misplacement of the catheter tip (Zatzkin and Irwin, 1964; Geipel, 1967) *e.g.* into the vagina.

Symptoms and survival have been linked with the amount of barium entering the circulation, and with the age and general health of the patient. Survival has also been related to the promptness of resuscitative measures, but the relative importance of this is dubious since death was immediate in all but two of the recorded fatalities.

Anatomically there is a free connection between the portal and systemic venous system via the haemorrhoidal plexus: the rectum draining into the portal circulation via the superior haemorrhoidal vein and inferior mesenteric vein, and via the inferior and middle haemorrhoidal veins into the systemic circulation. Either liver or lung acts as a filter, depending on whether the barium embolizes principally via the portal or systemic circulations respectively.

As regards early recognition of venous intravasation, Zatzkin and Irwin described a "Medusa head" pattern—a "tangled mass of tubular structures of barium density" radiating outward—and identified this pattern as indicating entry into the pelvic venous plexus.

The mode of entry of barium into the vascular system remains obscure. Various postulates have been put forward. In Zatzkin's and Geipel's cases there was an actual laceration of the vaginal mucosa to act as a portal of entry. However Roman *et al.* found no focal source, only erosions which appeared to be too superficial to be significant. They suggested that entry could have been through a small varix. Isaacs *et al.* suggested that when it occurred in ulcerative colitis it was due to a thinning of venous walls in the colonic mucosa.

All the cases hitherto described were women. The two survivors were rather younger (25 and 65) on average than the fatalities (mean age 74.4 years). The subject is briefly reviewed by Ansell (1976) who further suggests that minimal degrees of barium embolization may occur without symptoms.

CASE HISTORY

The patient, a white male born in 1892, presented in January 1965 with tenderness in the left iliac fossa and an extensive perianal fistula. A tentative diagnosis of diverticulitis was made. At operation for his fistula there was gross necrosis of the right wall of his anal canal and sphincter, and because of this destruction of his external sphincter he had a sigmoid colostomy the following week. The operation notes at the time comment that the sigmoid was "grossly oedematous, almost necrotic" but there was a good pulse in the sigmoid mesentery, Histology at that time showed chronic inflammatory granulation tissue, but no evidence of ulcerative colitis, diverticulitis or tuberculous disease.

He developed a large incisional hernia, which was repaired, and his colostomy was refashioned in October, 1965. The colostomy was brought out through separate stab incisions, the proximal loop to the left upper quadrant and the distal colostomy to the sub-umbilical region in the mid-line.

He remained reasonably well until 1979 when he presented with a history of passing blood and mucus from his rectal stump for several weeks. A barium enema was performed in May 1979. Initially barium was demonstrated tapering to a point, leaving a gap of several inches to the stoma at the skin surface. This appearance was constant despite the administration of Glucagon. No balloon catheter was used. A soft Foley catheter connected to a 50 ml syringe was introduced into the stoma (the balloon was uninflated) and barium was slowly injected. Horizontal shoot-through films were taken in an attempt to see if there was a demonstrable connection with the rectal stump (Fig. 1). These showed a sinuous collection of vessels around the stoma, with a linear structure running upwards, initially thought to be the ureter involved in a tumour mass.

The patient experienced no pain during the procedure. The examination was terminated and because of the possibility of a colo-ureteric fistula a limited IVU was performed. On the control film barium was demonstrated in the portal system of the liver (Fig. 2) and on reviewing the films the linear structure was identified as being in fact the inferior mesenteric vein (Fig. 3).

The patient was well until approximately 20 minutes later when he developed rigors which lasted about five minutes. These ceased spontaneously and although he was admitted to the ward for observation he developed no further symptoms or signs. He was given antibiotics and steroids prophylactically and was discharged some days later.

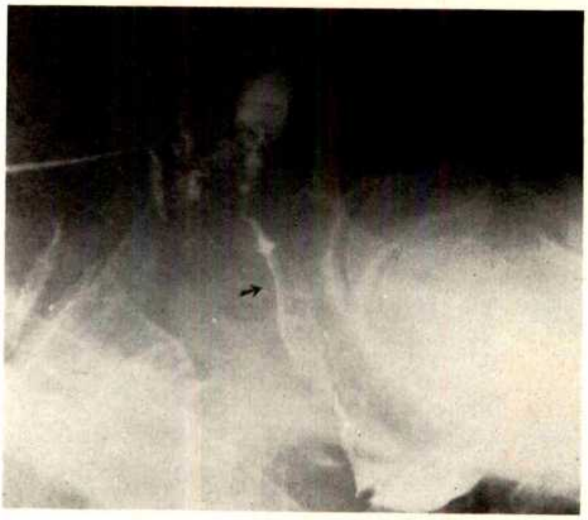


FIG. 1.

Horizontal shoot-through lateral film of the pelvis with catheters in rectum and stoma. Barium introduced per rectum stopped at the narrowing (arrow), later shown to be due to a carcinoma. Note sinuous vessels ("caput medusa") around stoma, with inferior mesenteric vein running cranially.

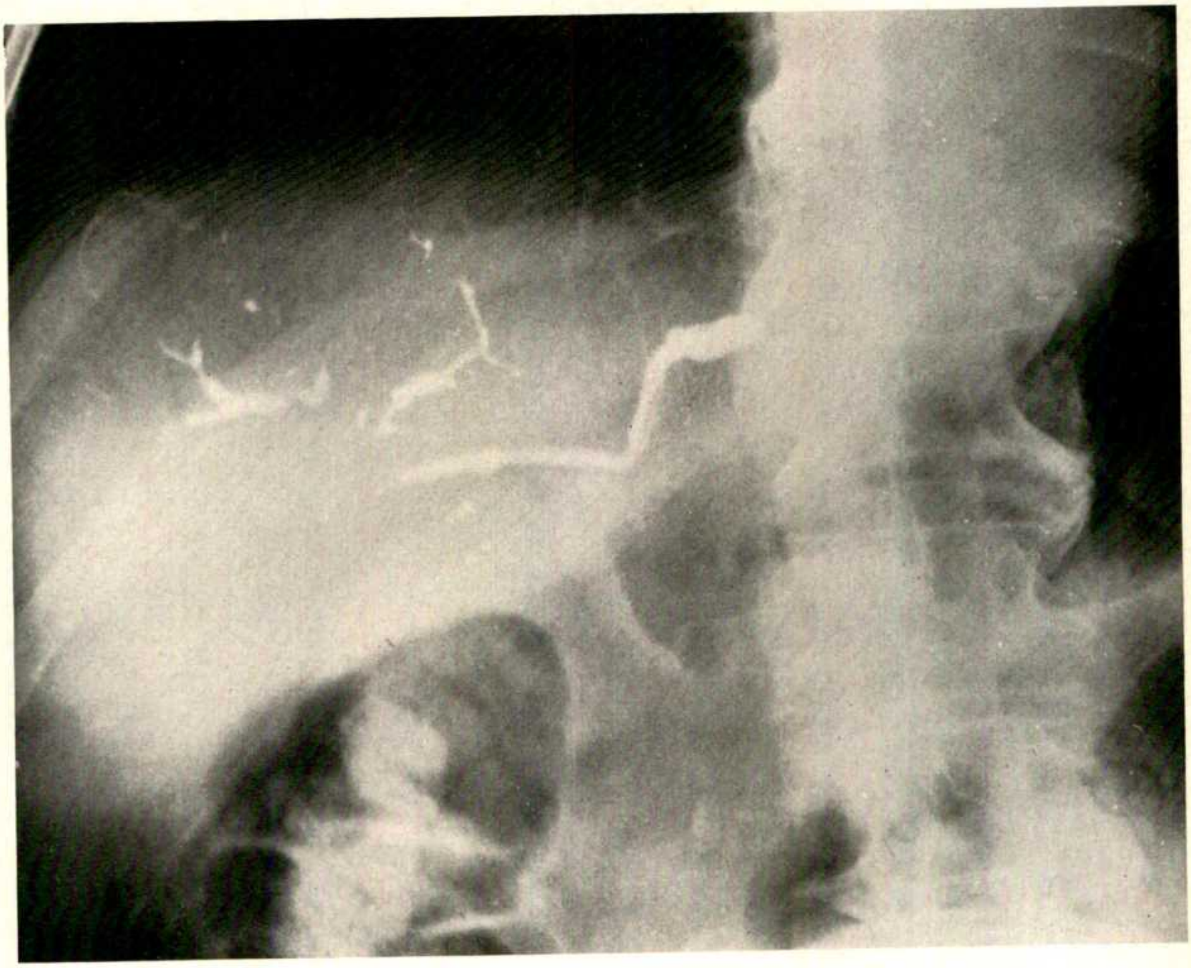


FIG. 2.
Control film showing barium in portal veins.

Subsequent sigmoidoscopy of his distal stump demonstrated a carcinona of the colon at 10 cm. Histology showed a poorly differentiated columnar cell carcinoma and he was started on a course of palliative radiotherapy.

At the time of writing, October, 1979, he remains alive and appears to have suffered no ill effects from his experience.

DISCUSSION

There are several aspects of note in this case. There was no evidence of underlying mucosal inflammation. By virtue of the technique of administration there was no question of increased intraluminal pressure, nor of complete obstruction. As can be seen on the illustrations there was a demonstrable connection between the stoma and the rectum. This was very narrow and we were unsure whether to attribute this to a tumour or an inflammatory mass, though subsequent endoscopy confirmed the presence of a carcinoma. There was no misplacement of the catheter and there was no significant trauma. There was also no evidence of any bleeding either during or after the procedure, and the haemoglobin remained unaltered. No discomfort was felt by the patient.

The patient was in a considerably older age group than the other two survivors; indeed at 86 he was the oldest patient in whom this complication has been described. It would appear that the major contributing factor in his survival was the very small amount of barium intravasated, and the fact that the barium demonstrably only entered the portal rather than systemic circulation—the liver acting as a filter to the inert barium. The initial and solitary episode of rigors probably indicated a septicaemia from bowel organisms introduced at the time of entry of the barium. Although it is difficult to quantitate the exact amount, about 5 ml at most entered the circulation.

1981, *British Journal of Radiology*, *54*, 72–74

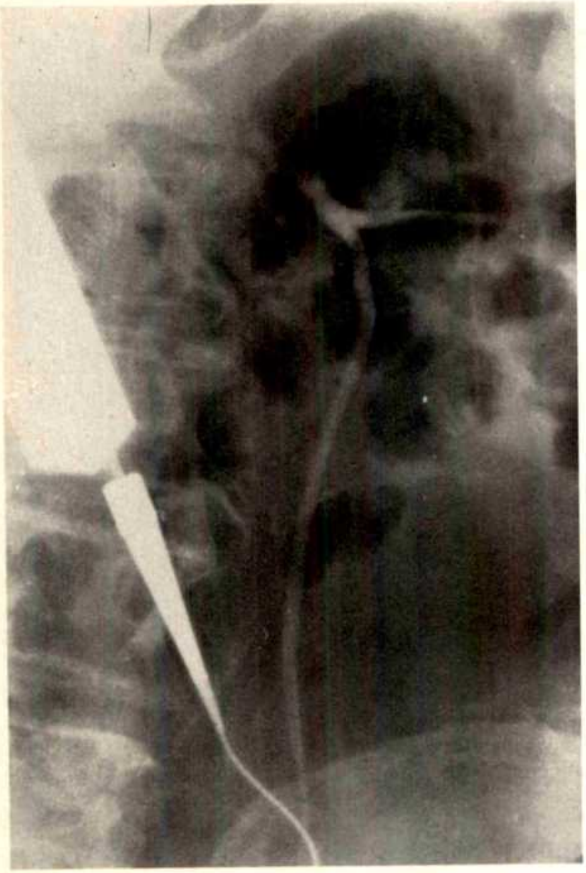


FIG. 3.
Vertical beam film showing inferior mesenteric vein opacified by barium.

It is of interest to note that the same sinuous "medusa-like" appearance described by Zatzkin and Irwin was seen in this case, which would support their contention that this is a valuable early indicator of probable venous intravasation.

As far as can be assessed this patient did not have any of the recognized predisposing causes for this rare complication.

We speculate that the combination of tumour and previous surgery must have distorted the vascular anatomy to allow this to happen.

REFERENCES

ANSELL, G., 1976. Venous intravasation. In *Complications in Radiology*, Chapter 16, pp. 352–354 (Blackwell, Oxford).

GEIPEL, A., 1967. Todlicher Zwischenfall nach Kontrastmitteleinlauf des Mastdarmes. *Deutsche Zeitschrift für die gesamte gerichtliche Medizin*, *59*, 255–295. (Quoted by Cove and Snyder).

ISAACS, I., NISSEN, R. and EPSTEIN, B. S., 1950. Non-fatal intravasation of barium. *New York State Journal of Medicine*, *50*, 332–334.

KAREN, J., COVE, J. and SNYDER, R. N., 1974. Fatal barium intravasation during barium enema. *Radiology*, *112*, 9–10.

NOVEROSKE, R. J., 1970. Barium sulphate into the heart from extra-peritoneal rupture of the rectosigmoid. *Journal of the Indiana Medical Association*, *63*, 32–33.

ROMAN, P. W., WAGNER, J. H. and STEINBACH, S. H., 1952. Massive fatal embolism during a barium enema. *Radiology*, *59*, 190–192

ROSENBERG, L. S. and FINE, A., 1959. Fatal venous intravasation of barium during a barium enema. *Radiology*, *73*, 771–773.

TRUEMNER, K. M., WHITE, S. and VANLANDINGHAM, H., 1960. Fatal embolisation of pulmonary capillaries. Report of a case associated with routine barium enema. *Journal of the American Medical Association*, *173*, 1089–1092.

ZATZKIN, H. R. and IRWIN, G. A. L., 1964. Non-fatal intravasation of barium. *American Journal of Roentgenology*, *92*, 1169–1172.

Duodenal ulcers causing obstructive jaundice and a mucocele of the gall bladder

By D. C. J. Fernando, M.R.C.P., D.M.R.D., T. D. Gopichandran, F.R.C.S., D.M.R.D.* and R. G. Kendrick, M.B., B.S., D.M.R.D.†

Department of Diagnostic Radiology, Plymouth General Hospital, Plymouth

(*Received July 1980*)

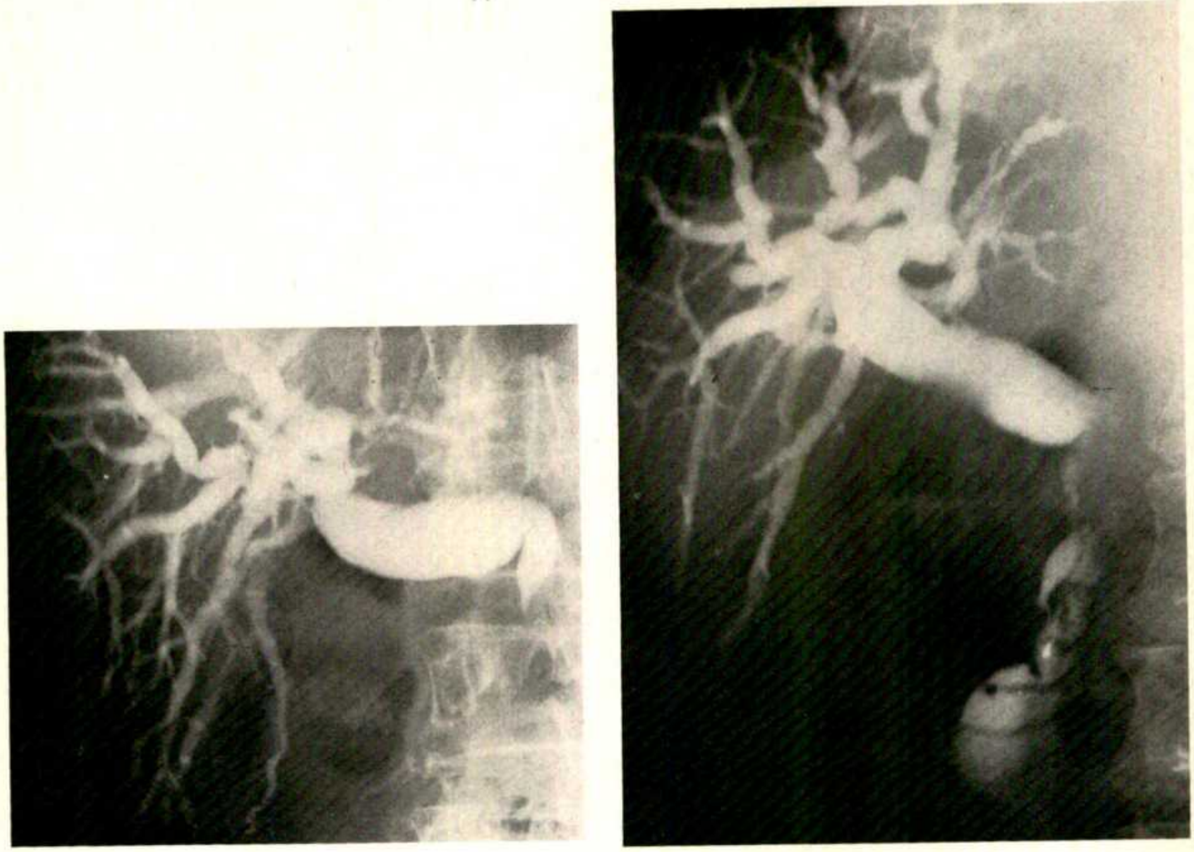
Duodenal ulceration is a rare cause of obstructive jaundice (six of 5240 cases at Mayo Clinic) (Onstad *et al.*, 1971). It is an even rarer cause of mucocele of the gall bladder. We wish to report a case in which both occurred simultaneously.

CASE REPORT

A 73-year-old male was admitted with a three-week history of epigastric pain. This was associated with loss of appetite. There was no relevant past history. On examination there was tenderness in the epigastrium and a smoothly enlarged, tender liver. The patient was obviously jaundiced. Blood tests revealed an obstructive jaundice (Alk. Phos. 180 KA units; Bilirubin 148 μmol/l; SGOT 65 Int. units/l), and there was an associated anaemia of 8.6 g/dl. Fine needle percutaneous transhepatic cholangiography revealed dilated intra-hepatic ducts and medial displacement of the common hepatic and common bile ducts. There was a long stricture

---

Present addresses: *Department of Diagnostic Radiology, St. James Hospital, Leeds.
†Department of Diagnostic Radiology, Westminster Hospital, London.



A FIG. 1. B

Percutaneous transhepatic cholangiogram showing dilatation of intra-hepatic ducts, dilatation and medial displacement of proximal common bile duct and stricture of lower common bile duct. (A) AP. (B) Oblique.

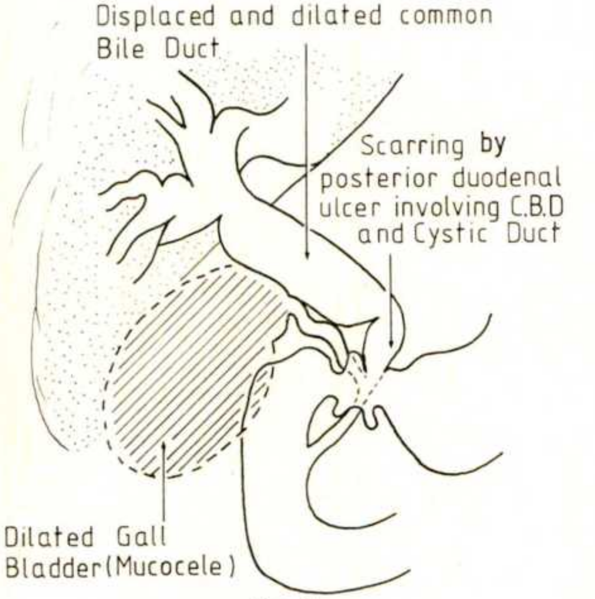

Displaced and dilated common Bile Duct
Scarring by posterior duodenal ulcer involving C.B.D and Cystic Duct
Dilated Gall Bladder (Mucocele)

FIG. 2.
Line drawing of operative findings.

of the common bile duct in its lower portion but no complete block. The gall bladder was not visualized (Fig. 1A, B). On these findings it was concluded that the most likely diagnosis was a carcinoma of the head of the pancreas. A primary carcinoma of the gall bladder was also considered as a less likely possibility.

Operative findings

At laparotomy a chronic anterior duodenal ulcer was found. This was adherent to a mucocele of the gall bladder which was displacing the common bile duct. There was low insertion of the cystic duct and it was completely obstructed by inflammation from a penetrating posterior ulcer which was also causing constriction of the lower common bile duct (Fig. 2). The anterior ulcer was dissected from the gall bladder and a pyloroplasty was fashioned. A vagotomy was also performed. The common bile duct was also dissected free and a choledochoduodenostomy was performed.

DISCUSSION

Anterior duodenal ulcers involving the fundus of the gall bladder are uncommon. Penetrating posterior duodenal ulcers involving the common bile duct and causing obstruction are even less common (Farrell, 1966; Sales, 1972; Stephenson *et al.*, 1952). We have been unable to find a case report of their

1981, *British Journal of Radiology*, *54*, 74–77

simultaneous occurrence. This case is also unusual in that there was, in addition, a low site of entry of the cystic duct to the common bile duct. This explained its involvement by the posterior ulcer and subsequent development of a mucocele of the gall bladder. The latter explained the marked displacement of the common bile duct seen at cholangiography.

Cholangiography was misleading as to the cause of the obstruction in this case. However, even had the duodenal ulceration been shown at a barium meal it is unlikely that the jaundice would have been attributed to it.

ACKNOWLEDGMENTS

We wish to thank Mr. C. Brown, Consultant Surgeon, Freedom Fields Hospital, Plymouth, under whose care this patient was admitted, for permission to publish this case.

REFERENCES

FARRELL, J. T., 1966. Obstructive jaundice secondary to duodenal ulcers. *American Journal of Gastroenterology*, *46*, 391–394.

ONSTAD, G. R., CHRISTENSEN, N. A. and SMITH, L. A., 1971. Jaundice as a complication of duodenal ulcer. *Surgical Clinics of North America*, *51*, 885–892.

SALES, J. E. L., 1972. Jaundice and duodenal ulceration. *British Journal of Clinical Practice*, *26*, 103–108.

STEPHENSON, S. L. Jr., RICE, M. L. and ROSSETT, N. E., 1952. Duodenal ulcer producing obstructive jaundice. *Gastroenterology*, *21*, 584–588.

Radiation pneumonitis in a patient exposed to asbestos

By R. F. U. Ashford, M.A., M.R.C.P., J. Maher, M.B., M.R.C.P.*, A. Drury, M.B., B.S. and D. Pickering, M.B., M.R.C.P.

Stanford Cade Department of Clinical Oncology, Westminster Hospital, London SW1

(Received February 1980 and in revised form July 1980)

The syndrome of radiation-induced lung damage follows pulmonary irradiation in roughly 10% of patients (Gross, 1977). Previous chemotherapy (Samuels *et al.*, 1976), radiotherapy (Kaplan and Stewart, 1973), and pulmonary consolidation and collapse (Bennett *et al.*, 1969) have all been shown to increase the incidence. We report the development of severe radiation pneumonitis in a patient with a history of exposure to asbestos. As far as we know this association has not been reported previously.

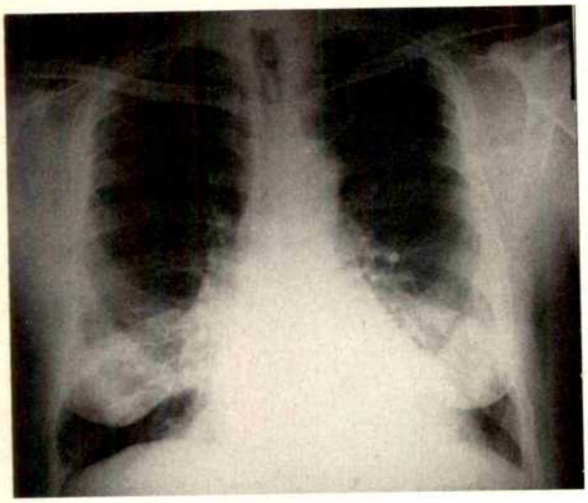


FIG. 1.
Pretreatment PA chest radiograph showing pleural plaque at left base and prominent nipple shadows.

CASE REPORT

A 58-year-old man was referred to our department for radiotherapy to a squamous cell carcinoma of the middle third of the oesophagus. There was no evidence of metastatic disease but he had a past history of hypertension and gout, had had a myocardial infarct in 1970 and was in atrial

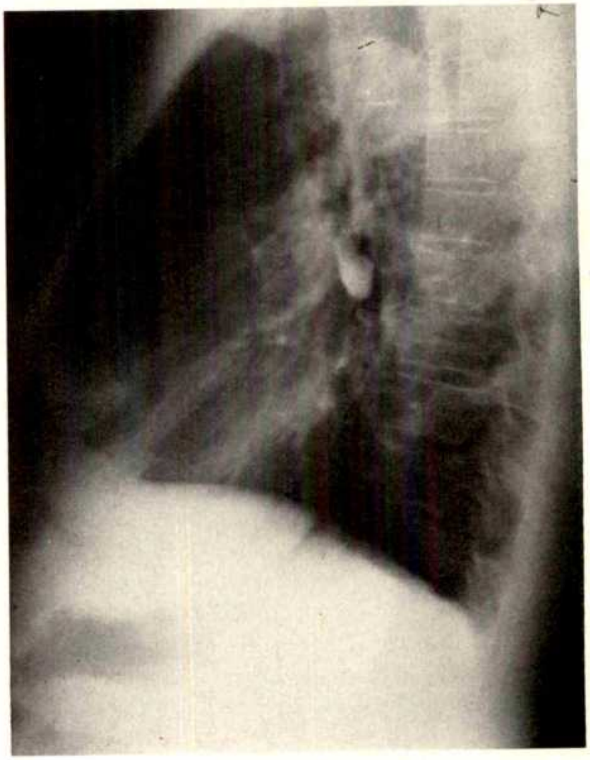


FIG. 2.
Pretreatment lateral chest radiograph.

---

*Present address: Radiotherapy Department, The Middlesex Hospital, London W1.

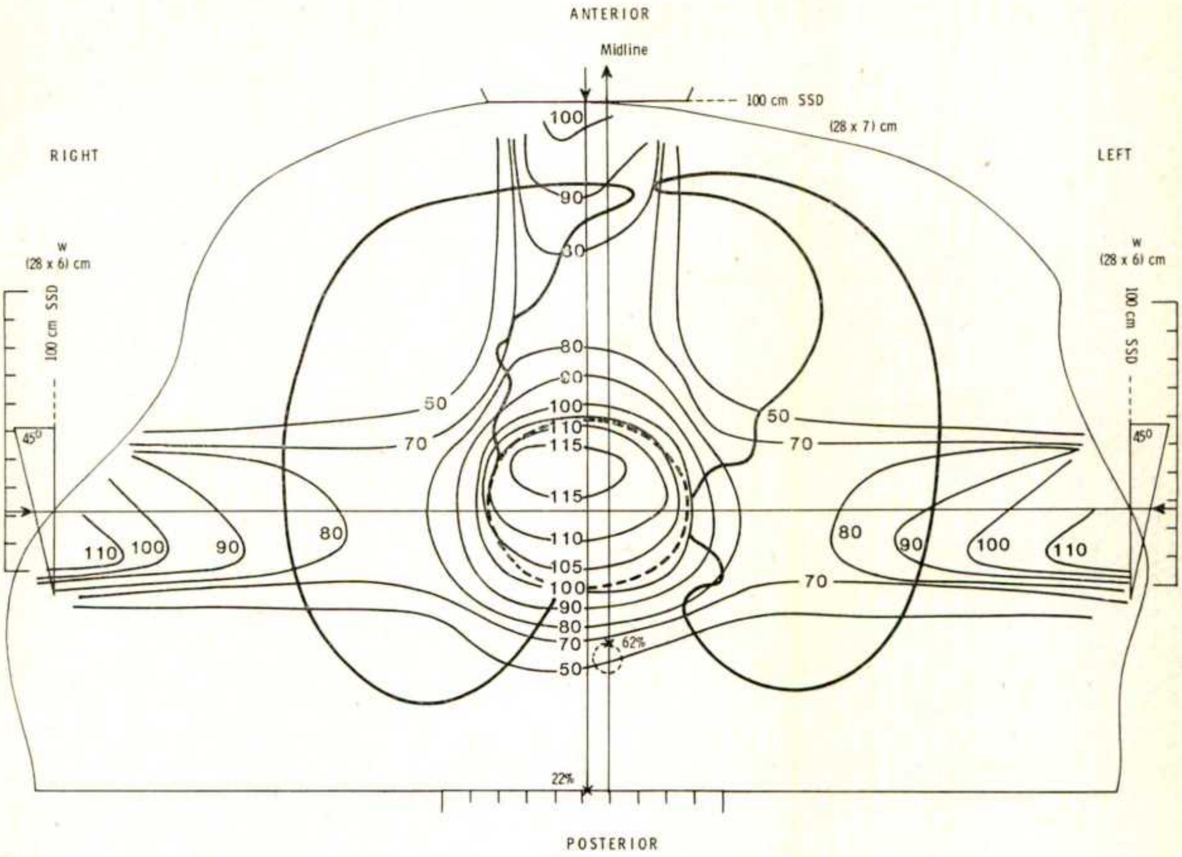


FIG. 3.

Treatment plan showing details of set up and isodose distribution. Heavy dotted line indicates treatment volume. Maximum spinal cord dose is 62%.

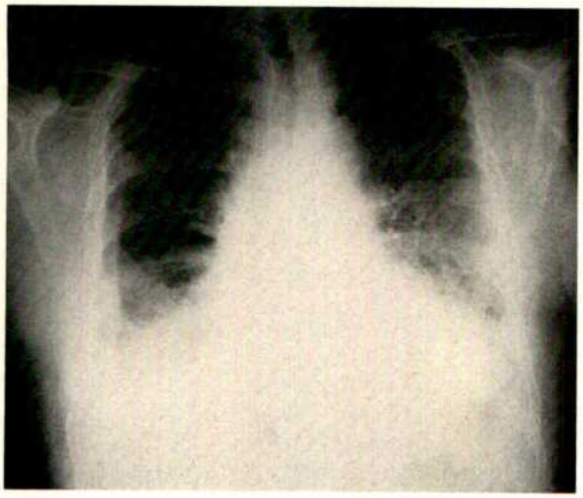


FIG. 4.

Post-treatment PA radiograph showing diffuse bilateral shadowing in middle and lower zones. There is also a right pleural shadow.

fibrillation. He smoked and drank to excess and had long-standing hepatomegaly from presumed alcoholic cirrhosis. For many years he had run an asbestos importing and fibreizing plant. Pretreatment chest radiographs (Figs. 1 and 2) showed upper lobe blood diversion and pleural plaques consistent with previous exposure to asbestos.

He received a total effective tumour dose (quoting on the 105% isodose curve) of 5400 cGy (rad) ^{60}Co γ rays to a 28×7 cm treatment volume comprizing the whole oesophagus. Treatment was given five days a week over 37 days by a three-field technique. The treatment plan is shown in Fig. 3. The calculated dose to the lungs within the fields varied between 3600 cGy minimum and 5150 cGy maximum.

His dysphagia resolved following radiotherapy and he became asymptomatic. However, a follow-up chest radiograph (Fig. 4) taken four months after completing radiotherapy showed extensive diffuse bilateral shadowing in the middle and lower zones. Lateral views (Fig. 5) showed the shadowing to be bounded by the margins of the treatment fields, strongly suggesting a radiation pneumonitis. Lung function tests showed a vital capacity of 2.36 litres (predicted 4.47) and FEV of 1.61 litres (predicted 3.43) consistent with a restrictive lung defect.

He was given Prednisolone 5 mg q.d.s. but developed right ventricular failure requiring hospitalization, vigorous diuretic therapy and discontinuation of his Prednisolone. His cardiac failure responded well to therapy and he was discharged. Symptoms of dysphagia recurred nine months after

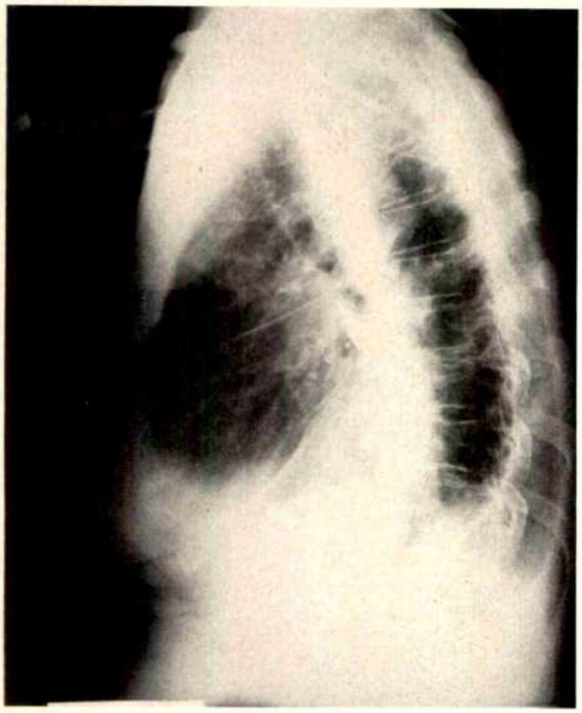


FIG. 5.

Post-treatment lateral radiograph showing the abnormal shadowing to be bounded by the margins of the treatment fields.

completing radiotherapy and there was an associated left recurrent laryngeal nerve palsy. At this stage a chest radiograph showed complete resolution of the pneumonitis. His condition deteriorated rapidly following the development of a tracheo-oesophageal fistula and he died shortly after. Detailed study of the lungs at autopsy revealed asbestos bodies associated with macrophages in many alveoli. In addition there were areas of subpleural fibrosis typical of asbestos exposure. However, there was no pulmonary interstitial fibrosis or evidence of radiation change, confirming that the pneumonitis had completely resolved.

DISCUSSION

It is well known that, as with any biological effect, the threshold for clinically detectable radiation-induced pulmonary damage varies from individual to individual. A number of factors have been shown to lower this threshold. Phillips and Margolis (1972) and Phillips *et al.* (1975) have shown increased lethality in mice when pulmonary irradiation is given following actinomycin D, cyclophosphamide and Vincristine. There was also a suggestion that corticosteroids offered some protection and that rapid steroid withdrawal could precipitate death. In man there is evidence of enhanced pulmonary toxicity following a number of cytotoxic agents, notably bleomycin (Samuels *et al.*, 1976).

As expected, previous pulmonary radiotherapy predisposes to acute radiation pneumonitis, as reported by many authors, most recently by Kaplan and Stewart (1973). They found that reirradiation of the mediastinum for Hodgkin's disease necessitated by inadequate treatment resulted in radiation pneumonitis nearly three times as frequently as in patients irradiated for the first time.

The effect of pre-existing pulmonary disease has also been studied by several authors. Gillam *et al.* (1964) showed that the incidence of radiation-induced pulmonary damage was not increased in chronic bronchitics irradiated for carcinoma of the bronchus. However, Bennett *et al.* (1969) reported seven cases of bilateral radiation pneumonitis following radiotherapy for carcinoma of the bronchus. Co-existing lung disease, mainly consolidation and collapse, was considered contributory, as only one of these patients had normal lungs (apart from the carcinoma) before treatment.

We can find no reports of radiation pneumonitis developing in patients with asbestosis. It is important to note that this is the most florid case of radiation pneumonitis seen in our department for some years. In addition, we have not seen pneumonitis in other patients treated for carcinoma of the oesophagus using this three-field technique. While coincidence is possible, we feel it is more likely that the presence of asbestos bodies within this patient's alveoli in some way magnified the effect of irradiation. Their presence could increase lung density and therefore local radiation dose, which could then exceed the threshold for clinical manifestations. Alternatively, radiation damage to the alveolar lining could enhance the irritant effect of asbestos bodies. Fortunately our patient had sufficient unaffected lung to prevent serious respiratory difficulties and furthermore the pneumonitis resolved completely. We believe patients with a history of asbestos exposure, whose lungs are irradiated, are worthy of close scrutiny. Radiation pneumonitis with its potentially serious consequences might be more frequent in this population and in addition complete resolution may not be the rule.

CONCLUSION

Asbestosis could be another factor that may contribute to radiation pneumonitis. It is, therefore, important to enquire about asbestos exposure, especially as the incidence of malignancy is increased in these patients (Longley, 1978). In considering radiotherapy to an asbestos-exposed patient a possible increase in the lung's sensitivity to radiation should be remembered when planning and deciding dosage.

ACKNOWLEDGMENTS

Our thanks to Dr. K. A. Newton for his help and for permission to report the case; to Mr. R. A. D. Booth who referred the case; to Dr. J. H. O. Earle who performed the post-mortem, and to Dr. D. H. Trapnell for his help with the manuscript.

REFERENCES

BENNETT, D. E., MILLION, R. R. and ACKERMAN, L. V., 1969. Bilateral radiation pneumonitis, a complication of the radiotherapy of bronchogenic carcinoma. *Cancer*, *23*, 1001–1018.

GILLIAM, P. M. S., HEAF, P. J. D., HOFFBRAND, B. I. and HILTON, G., 1964. Chronic bronchitis and radiotherapy of the lung. *Lancet*, *i*, 1245–1248.

GROSS, N. J., 1977. Pulmonary effects of radiation therapy. *Annals of Internal Medicine*, *86*, 81–92.

KAPLAN, H. S. and STEWART, J. R., 1973. Complications of intensive megavoltage radiotherapy for Hodgkin's Disease. *National Cancer Institute Monograph*, *36*, 439–444.

LONGLEY, E. O , 1978. Dust disease of the lungs. *Medical Journal of Australia*, *2*, 474–476.

PHILLIPS, T. L. and MARGOLIS, L., 1972., Radiation pathology and the clinical response of lung and oesophagus. *Frontiers of Radiation Therapy and Oncology*, *6*, 254–273.

PHILLIPS, T. L., WHARAM, M. D. and MARGOLIS, L. W., 1975. Modification of radiation injury to normal tissues by chemotherapeutic agents. *Cancer*, *35*, 1678–1684.

SAMUELS, M. L., JOHNSON, D. E., HOLOYE, P. Y. and LANZOTTI, V. J., 1976. Large dose bleomycin therapy and pulmonary toxicity—a possible role of prior radiotherapy. *Journal of the American Medical Association* *235*, 1117–1120.

Book reviews

Atlas of Disease and Special Examination of the Breast. By V. Barth, pp. 198, 1979 (YB Medical Publishers, Chicago, London), £59·00.
ISBN 0–8151–0418–9

Dr. Barth has a wide experience of breast pathology and mammography so that he is ideally suited to produce a book devoted mainly to the correlation of radiological findings in breast disease and the morphological and histological features of those diseases. This translation is a welcome addition to the English literature on mammography and associated diagnostic techniques.

The work is described as an atlas of diseases of the breast. It is an excellent atlas but also contains accounts of clinical examination, mammography, specimen radiography, galactography, pneumocystography, electronic and plate thermography and cytological examination. In addition the features of benign and malignant diseases are discussed.

The volume consists of a comprehensive collection of mammograms, ductograms and pneumocystograms of the various breast conditions with the corresponding morphological specimens and histology. Thermographic findings are also illustrated in many cases. Perhaps the most valuable feature of the book is the account of microradiography of the breast—the first English account of this interesting topic. Dr. Barth has written a German monograph on this subject previously and many of the cases and diagrams are reproduced in this atlas also.

The book may be regarded as being expensive but a publication of this quality cannot be produced cheaply. The reproductions of the illustrations are superb and the format is excellent. It is highly recommended to doctors of all disciplines interested in the management of breast disease.

I. H. GRAVELLE.

Differentialdiagnose seltener Lungenerkrankungen im Röntgenbild. By K. Musshoff, J. Weinreich and H. Willmann. 1979. pp. vii+324. (Springer-Verlag, Berlin/Heidelberg/New York). DM.190/$104.50.
ISBN 3–540–09297–8

This book is written in the form of a radiological atlas of a large number of different radiological patterns of a variety of uncommon and less common disorders. The authors have separated the various groups under different patterns of radiological shadows rather than under varying pathological disorders. The main groups comprise lesions of consolidation, multiple fine nodular lesions, solitary coin lesions, larger masses, linear shadows, mediastinal and hilar shadows and unequal aeration, with particular emphasis on air trapping. The radiographs are of very good quality, but unfortunately reproduced as positives which makes for some difficulty of interpretation. Each radiograph is annotated by a good clinical history, clinical findings and radiological description. Nomenclature, however, creates some difficulty since the radiological descriptions in German don't easily relate to the English nomenclature, so that a non-German-speaking radiologist would have problems in understanding the radiological reports.

The literature is quoted quite widely, but some of the papers are out of date, which is unfortunate since there have been important new developments in the last few years, particularly in disease processes producing diffuse and/or interstitial shadows.

The production of the book is of a high standard and quality, but its usefulness to the English reader is somewhat limited since it does not provide a real systematic approach to the problem and only covers the field in a superficial way.

R. E. STEINER.

1981, *British Journal of Radiology*, *54*, 78–79

Short communications

Rib artefact in computed tomography

By A. K. Dixon, M.A., M.R.C.P., F.R.C.R.*

Department of Diagnostic Radiology, St Bartholomew's Hospital, London EC1

and I. G. Wylie, M.B., F.R.C.S., F.R.C.R.

Department of Diagnostic Radiology, The London Hospital, London E1

(*Received August 1980*)

Nodules seen at computed tomography (CT) in the periphery of the lung are frequently due to metastases. However, CT is not tissue-specific, and both granulomata and benign pleural-based lymphoid aggregates may be responsible for nodules (Schaner *et al.*, 1978). An additional source of confusion may be a small portion of bone from an adjacent cut causing similar appearances due to partial volume effect. This is sometimes seen in the upper zone where a portion of the medial end of clavicle or first rib may cause an artefact shadow in the lung. However this possibility should also be considered elsewhere in the thorax.

Case report

A 43-year-old male patient was referred for a CT scan of the chest to exclude pulmonary deposits from a chondrosarcoma. The primary tumour had arisen from the region of the left intervertebral foramen at the T3 T4 level. The patient had had a decompressive laminectomy and had received local radiotherapy. His chest radiograph was normal at the time of scanning and remains so some 18 months later.

Scans were obtained at 1 cm intervals on an EMI 5005 scanner which has a 20 s scan time. Cuts of 1.3 cm thickness are produced. The lungs appeared clear except for one cut where two symmetrical anterior peripheral opacities were noted (Fig. 1).

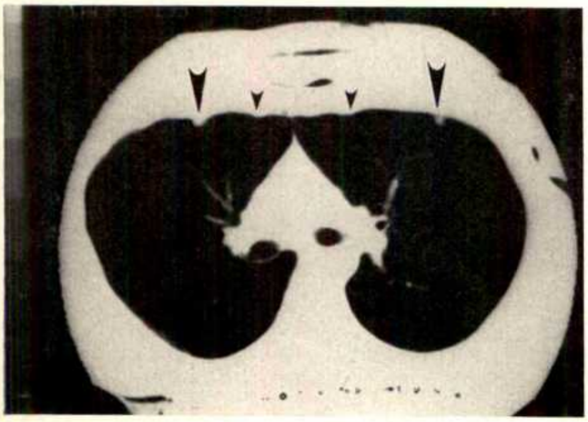


FIG. 1.

CT scan at a level just below the carina at lung settings showing bilateral symmetrical anterior peripheral opacities (large arrowheads). The small arrowheads point to the position of the internal mammary arteries.

Discussion

The appearances could easily have been mistaken for lung metastases but the symmetry suggested an anatomical cause. The opacities were too far lateral to be the normal internal mammary arteries. Close viewing of this and the adjacent superior cut on the independent console at different settings revealed that these shadows were due to a small portion of the rib from the adjacent cut being caught in the 1.3 cm scan thickness (Figs. 2, 3 and 4). A small portion of bone density material in the cut will simulate a lesion of soft

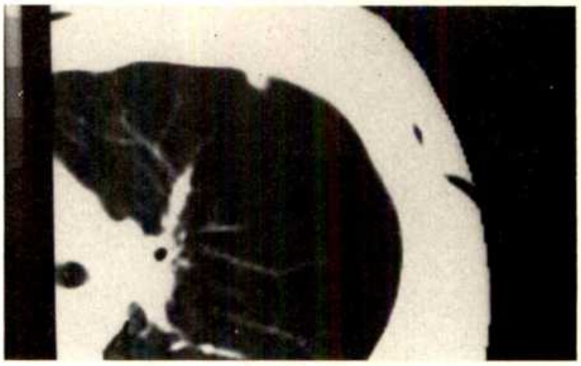


FIG. 2.

Close-up view of the lesion in the left hemithorax. Appearances similar to a peripherally placed metastasis.

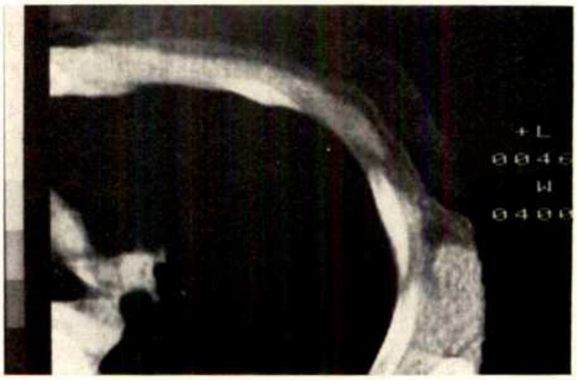


FIG. 3.

Soft tissue setting of the adjacent superior cut which clearly shows the responsible rib.

---

*Present address and address for communication: Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

Short communication

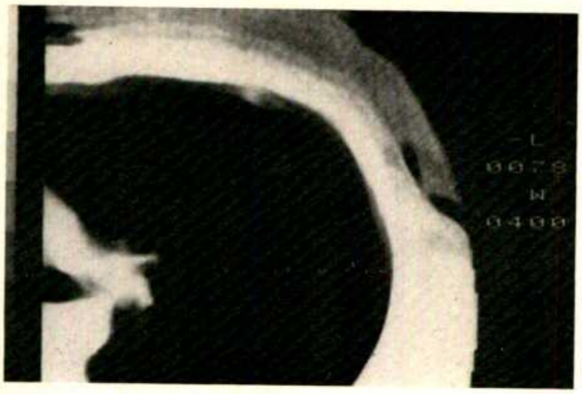


FIG. 4.

Composite picture obtained on the independent viewing console by averaging out the information from the adjacent cuts. This shows the exact site of the artefact in relation to the rib above.

tissue density by partial volume effect. This occurrence has been seen occasionally in children where the curvature of the thorax is relatively more pronounced. Clearly, in some patients the indentation into the parietal pleura by the rib will be more prominent than in others. No doubt this rib artefact will be less of a problem with scanners capable of producing thinner cuts. Hopefully misinterpretation can be avoided by careful viewing of adjacent cuts at different levels and window widths.

ACKNOWLEDGMENTS

We are grateful to the Trustees of St. Bartholomew's Hospital for their generosity in purchasing the scanner and supporting one of us (AKD). We would like to thank Dr. Kelsey Fry for his advice.

REFERENCE

SCHANER, E. G., CHANG, A. E., DOPPMAN, J. L., CONKLE, D. M., FLYE, M. W. and ROSENBERG, S. A., 1978. Comparison of computed and conventional whole lung tomography in detecting pulmonary nodules: a prospective radiologic-pathologic study. *American Journal of Roentgenology*, *131*, 51–54.

A comparative trial of three oral cholecystographic contrast media—iocetamic acid, iopanoic acid and sodium ipodate

By A. Cargill, M.R.C.P., F.R.C.R. and W. Hately, F.R.C.P.(Ed.), F.R.C.R.

Department of Diagnostic Radiology, The London Hospital, London E1 1BB

(*Received January 1980 and in revised form August 1980*)

Three hundred consecutive patients referred for oral cholecystography were randomly allocated to one of three groups: iocetamic acid (Cholebrin) (95), iopanoic acid (Telepaque) (101) and sodium ipodate (Biloptin) (104). Following routine preparation for the study, a control film was taken. Where bowel preparation was adequate, each patient was given a numbered packet containing 3 g of contrast medium which was taken on the evening before the formal oral cholecystogram. At the beginning of the study—normally 14 hours following ingestion of the contrast material—the supervising radiologist checked the patient's weight and confirmed that both the aperient and the oral cholecystographic agent had been taken. Contrast related symptoms were assessed using a standard questionnaire and, following this, a routine series of coned films of the gall bladder area were obtained. These included a prone oblique, a supine oblique and an erect film, as well as a repeat prone oblique view 30–40 minutes after a fatty meal. The gall bladder did not opacify in 55 patients given a single dose of contrast, and of these 33 had a repeat study with a double-dose a week after the initial examination.

RESULTS

Radiological assessment

Gall bladder opacification (Table I) was classified as good in 42% of patients given iocetamic acid, 38% of those given iopanoic acid and 32% receiving sodium ipodate. The differences in the results classified as good were not statistically significant, as assessed by the χ^2 test ($0.5 > P > 0.1$).

There was no correlation between weight and non-visualization of the gall bladder. The mean weight of 168 weighed cases whose gall bladder opacified was 68.95 kg, as compared with a mean weight of 70.31 kg in the 28 weighed cases whose gall bladder did not opacify. The difference was not significant ($P > 0.5$). Gall stones were demonstrated in 51 patients.

Opacification of the common bile duct before a fatty meal (Table II) occurred in 24% of the iocetamic acid cases, 36% of the iopanoic acid cases and 20% of the sodium ipodate cases. The superiority of iopanoic acid was significant at the 0.05 level when a χ^2 test was applied ($0.5 > P > 0.02$).

Opacification of the common bile duct 30–40 minutes after a standard fatty meal given to 256 patients (Table III) occurred in 47% of the iocetamic acid group, 52% of the iopanoic acid group and 44% of the patients taking sodium ipodate. These differences were not statistically significant ($P > 0.5$). The giving of a fatty meal increased the proportion of patients in whom the common bile duct was visualized by 53%. (123 patients in total, Table III, compared with 80, Table II).

Double dose studies (Table IV): 33 of the 54 patients whose gall bladders did not opacify initially were re-examined following a double-dose of contrast given a week after the first study. The biliary tree was visualised in a proportion of these cases, but the reasons for this are obscure (Berk, 1970). The differences in the rates of opacification of the gall bladder were not significant in the three groups ($\chi^2 = 1.8$ d.f. $= 6$ $P > 0.5$).

TABLE I

GALL BLADDER OPACIFICATION

	Cholebrin	Telepaque	Biloptin	Total
Nil	16	22	16	54
Poor	20	14	24	58
Fair	19	27	31	77
Good	40	38	33	111
TOTAL	95	101	104	300

$\chi^2 = 7.141$ d.f. $= 6$. $0.5 > P > 0.1$

TABLE II

COMMON BILE DUCT OPACIFICATION—BEFORE FATTY MEAL

	Cholebrin	Telepaque	Biloptin	Total
Absent	72	65	83	220
Present	23	36	21	80
TOTAL	95	101	104	300

$\chi^2 = 6.66$ d.f. $= 2$. $0.05 > P > 0.02$

TABLE III

COMMON BILE DUCT OPACIFICATION—AFTER FATTY MEAL

	Cholebrin	Telepaque	Biloptin	Total
Absent	43	40	50	133
Present	38	45	40	123
TOTAL	81	85	90	256

$\chi^2 = 1.33$ d.f. $= 2$ $P > 0.5$

Unabsorbed gut residues (Table V): in 60.5% (181) of the patients, no contrast residues were seen on the radiographs. Moderate residues were present in 22.5% (68), and gross residues were seen in 17% (51). Residues did not interfere with the assessment of the appearances of the gall bladder and the common bile duct. They were most often seen with iopanoic acid and least often with sodium ipodate.

Side effects (Table VI) most commonly complained of in response to direct questioning were nausea, headache, dizziness and diarrhoea. Headache was slightly more frequent in patients taking sodium ipodate ($\chi^2 = 5.164$ d.f. $= 2$ $0.01 > P > 0.05$), but there was no important difference in the incidence of the other symptoms reported by the three groups of patients. Only one patient spontaneously complained of abdominal discomfort, and there were no reports of flatulence or an unusual taste in the mouth.

COMMENT

Iocetamic acid (Cholebrin), sodium ipodate (Biloptin) and iopanoic acid (Telepaque) showed no significant differences in their ability to opacify the gall bladder. Contrast related symptoms are common, but the incidence of any particular symptom is highly dependent on the type of questionnaire used (Owen and Lavelle, 1978; Fielding and Whitehouse, 1979), and on the method of assessment. Unabsorbed contrast residues did not interfere with interpretation of the appearances of the biliary tree. These findings suggest that the cheapest of the three contrast materials would be satisfactory.

TABLE IV

GALL BLADDER OPACIFICATION (NON-OPACIFIERS)—DOUBLE DOSE

	Cholebrin	Telepaque	Biloptin
Nil	7	6	7
Poor	2	2	3
Fair	1	1	0
Good	1	2	1
TOTAL	11	11	11

$\chi^2 = 1.8$ d.f. $= 6$. $P > 0.5$ N.S.

TABLE V

GUT CONTRAST RESIDUES

	Cholebrin	Telepaque	Biloptin	Total
Nil	63	33	85	181
Moderate	16	39	13	68
Gross	16	29	6	51
TOTAL	95	101	104	300

$\chi^2 = 10.1185$ d.f. $= 2$. $0.001 > P$

TABLE VI

SYMPTOMS

Symptom	No. of Patients			
	Cholebrin	Telepaque	Biloptin	Total
Nausea	10	6	10	26
Headache	7	4	13	24
Dizziness	5	6	7	18
Diarrhoea	2	12	2	16
Polyuria	5	5	4	14
Dysuria	0	7	3	10
Oliguria	2	2	4	8
Vomiting	3	0	1	4
Pruritus	1	1	1	3
Urticaria/Rash	1	0	2	3
Wheeze	0	0	1	1

ACKNOWLEDGMENTS

The authors wish to thank Mr. Ian Pugh and his radiographic and clerical colleagues for their help. Thanks are also due to Miss Janet Mutch who typed the manuscript, to Napp Laboratories for providing supplies of contrast media, and to Mr. Richard Pugsley for his assistance with the statistics.

REFERENCES

BERK, R. N., 1970. The consecutive dose phenomenon in oral cholecystography. *American Journal of Roentgenology*, *110*, 230–234.

FIELDING, J. A. and WHITEHOUSE, G. H., 1979. A comparative trial of two oral cholecystographic contrast media – iocetamic acid (Cholebrin) and iopanoic acid (Telepaque). *Clinical Radiology*, *30*, 45–48.

OWEN, J. P. and LAVELLE, M. I., 1978. Comparative study of iocetamic acid and calcium ipodate in the visualisation of the gall bladder and common bile duct. *Clinical Radiology*, *29*, 535–540.

1981, *British Journal of Radiology*, *54*, 81–84 JANUARY 1981

Proceedings of the MRC Committee on Protection against Ionizing Radiations

Radiobiology forum on non-stochastic effects of ionizing radiations held on March 4, 1980

THE RECOMMENDATIONS OF THE INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION (ICRP)

By J. Vennart

MRC Radiobiology Unit, Harwell, Oxon

In its Publication 26, ICRP considered stochastic and non-stochastic effects of ionizing radiations. Stochastic effects are those for which the probability of an effect occurring, rather than its severity, is regarded as a function of dose without threshold of which the chief to be considered are cancer in irradiated individuals and hereditary diseases in their descendants. Non-stochastic effects are those for which the severity of the effect varies with the dose and for which a threshold may therefore occur. Some of these are specific to particular tissues, *e.g.* cataract, others may arise in blood vessels and connective tissues which are common to most organs of the body. The aims of the recommendations are to prevent non-stochastic effects and limit the probability of stochastic effects to an acceptable level.

ICRP recommends that all doses be kept as low as reasonably achievable and that doses to individuals should not exceed certain limits. For uniform irradiation of the body of a worker the limit is 0.05 Sv (5 rem), and for a member of the public 5 mSv (0.5 rem) in a year. The limits are based on comparisons of the risks of radiation-induced fatal cancer and serious hereditary disease with those of fatalities in other industries and in everyday life respectively. Non-uniform irradiation of the body is limited so that the total risk of stochastic effects in all the tissues irradiated does not exceed those from appropriate limits on uniform whole-body irradiation. To prevent non-stochastic effects ICRP recommends for a worker limits of 0.3 Sv (30 rem)* in the lens and 0.5 Sv (50 rem) in all other tissues; for a member of the public the limit is 0.05 Sv (5 rem) in any tissue.

ICRP gives estimates of the risk of radiation-induced cancer and hereditary disease from which can be derived the dose equivalent in any tissue that gives the same risk as the total risk from uniform irradiation of the body to its appropriate annual limit on dose equivalent. For many tissues of low sensitivity to radiation-induced cancer, such as thyroid and bone, these dose equivalents are greater than the annual limit used to prevent non-stochastic effects. In consequence, the intake of some radioactive materials, such as ^{131}I and ^{239}Pu, are limited by consideration of non-stochastic effects, *e.g.* in thyroid and bone respectively. Estimates of the risks of radiation-induced cancer and hereditary disease are much more reliable now than heretofore; data on non-stochastic effects are less well founded. Therefore, in view of the overriding importance of non-stochastic effects in some circumstances, it is important to review the data available on these effects.

THE RESPONSE OF RAPIDLY DIVIDING TISSUES TO ACUTE OR PROTRACTED EXPOSURE TO IONIZING RADIATIONS

By S. B. Field

MRC Cyclotron Unit, Hammersmith Hospital, London

It has been postulated that there will be a "threshold" for non-stochastic damage. However, the "threshold" will depend on the apparatus used for its measurements. For example, damage to mitochondria in rat intestinal cells is demonstrable by electron microscopy after a fraction of a gray whereas 5–10 Gy are required for gross changes. It is also important to distinguish between transient and permanent effects.

After irradiation, cells and tissues are capable of various repair processes, in particular recovery from sublethal damage (SLD) and repopulation. Recovery from SLD will increase the dose required to produce a given effect with many fractions or by low dose rate, compared with a single treatment, by a factor of between three and ten. With rapidly dividing tissues, such as skin and gastro-intestinal tract, cellular repopulation will further increase the threshold dose for fractionated or low-dose rate treatments such that very large doses are required to produce measurable changes in these tissues. Growing cartilage and bone are more sensitive. In animals the threshold for stunting is between 0 and 1 Gy with 0.2–0.3 Gy required for 1% stunting. In man the approximate threshold for a detectable change in growing bone is about 3 Gy up to one year of age increasing to 10 Gy by two years (r.e.t. doses taken from radiotherapy data).

For fast neutrons, repair of sublethal damage is much less than for X rays so that the dose to produce a given reaction is not much increased by fractionation and the RBE increases with decreasing dose. However, repopulation after neutrons is not thought to be significantly different from that after X rays, so even with neutrons large doses are required to produce reactions in rapidly dividing tissues if irradiation is protracted.

RADIATION EFFECTS ON SLOWLY PROLIFERATING TISSUES

By J. Denekamp

Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex

In considering the non-stochastic effects of radiation, *i.e.* the graded response with dose, we are faced with the problem of defining what response is important. Threshold doses exist for most effects but these may tell us more about the sensitivity of the method of detecting damage than about the sensitivity of the cells or organs. In mice, lethality (LD$_{50}$) or gross functional defects are studied, whereas for protection purposes in man much lower levels of damage should be considered, but little or no information is then available.

---

*Reduced to 0.15 Sv after the meeting of ICRP in Brighton, March 1980.

Radiation damage in slowly proliferating tissues often takes the form of fibrosis, which may be a primary event or be secondary to loss of radiation-killed parenchymal cells, or tertiary to killing of vascular/connective tissue cells which lead indirectly by nutrient failure to death of the parenchymal cells. The damage occurs later than in rapidly dividing tissues because there is a long delay before the next mitosis at which radiation death will be manifested (months or years).

In animal studies, slowly proliferating tissues have a threshold of 10–20 Gy (1–2 krad) for functional damage. There may then be a gradual increase in damage without it being life threatening (*e.g.* by a factor ~2 in the bladder), or the loss of function may become lethal over a small dose range (*e.g.* in the lung).

Clinical data for tolerance of normal tissue to fractionated irradiation have been accumulated over the past 50 years in radiotherapy. Different tissues have different sensitivities and these depend critically on the volume irradiated. In general, slow turnover tissues are neither more nor less sensitive than rapidly proliferating tissues: the sparing effect of fractionation is probably more an effect of biochemical repair processes than of reparative compensatory proliferation in these slowly proliferating tissues.

EFFECTS OF RADIATION ON FERTILITY

By M. F. Lyon

MRC Radiobiology Unit, Harwell, Oxon

In both male and female the effects of radiation on fertility vary with species and among individuals within a species, as well as depending on germ-cell stage and the age of the individual at treatment. In the male, early stages of gametogenesis are most sensitive, leading to temporary sterility or oligospermia after moderate doses and permanent effects after high doses. The human male is very sensitive with temporary aspermia after 35–50 cGy (rad) acute or fractionated exposures. In the mouse, chronic irradiation at only a few rad per week will impair fertility, and as man is more sensitive the non-stochastic limit of 0.5 Sv (50 rem) per year could produce deleterious effects. The human female is relatively resistant to radiation sterilization compared with other species. Acute and fractionated doses up to about 150 cGy (rad) do not appear to impair fertility, but above 200 cGy temporary or permanent amenorrhoea and sterility occur in some individuals, with total sterility above about 1200 cGy (rad) in young women. Women over 40 and also probably young children are more sensitive. In the mouse, dose protraction or multiple small fractionation has a marked sparing effect on female fertility, and hence in the human female permitted doses and diagnostic exposures are unlikely to have any deleterious effect on fertility.

NON-STOCHASTIC EFFECTS IN THE HAEMOPOIETIC SYSTEM

By L. G. Lajtha

Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester

The clsssical radiation response giving the well-known transient depression in the peripheral blood values represents a dose-dependent temporary risk period from which recovery can take place. However, the recovery is, in a sense, "superficial" because on analysis the pluripotent stem cell population indicates that the recovery is usually on a sub-optimal "plateau" lasting for several months in the mouse. This is only detectable in the mouse following doses of about 50 cGy (rad) or over, and is compensated as far as mature cell production is concerned by increased amplification during transit in the maturing transit cell populations.

It is noteworthy that the stem cell effect appears to be dose-rate independent in the dose-rate range of 10 Gy (1000 rad) per hour down to about 2 cGy (rad) per hour—but only until a depopulation in the stem cells of about 5% of the normal values. The mainly non-cycling stem cell population begins to cycle by then and the sterilization rate per cell cycle is, as expected, dose-rate dependent between the ranges of 2–6 cGy (rad) per hour. The recovery, like in the case of acute radiation, is incomplete and stays at sub-optimal plateau, the level of which is dose dependent and accumulated-dose dependent (due to the long duration of each sub-optimal plateau). Like in the case of the acute radiation, the sub-optimal stem cell levels are compensated by increased amplification during transit. Consequently the blood count values during and following irradiation do not give a real picture of the haemopoietic status of the host.

NON-STOCHASTIC EFFECTS ON ENDOCRINE ORGANS

By E. E. Pochin

National Radiological Protection Board, Harwell, Oxon

The non-stochastic effects of radiation on human endocrine organs are likely to be of greatest practical importance in regard to the thyroid, in view of the selective concentration of radioiodine in the gland. There is also more reliable quantitative information about these effects in man than in the case of other glands.

Rapid destruction of tissue with loss of subsequent thyroid function occurs in man when absorbed doses of 400 to 500 Gy are delivered within a few days to the gland by ^{131}I. Discharge of labelled cell contents is largely complete within a few days of these doses being received.

Absorbed doses of from 25 to 65 Gy from fractionated external exposure have been reported to cause a much slower loss of function, particularly in children, with complete failure developing within a few months or years in some cases. After treatment of the overactive gland, myxoedema is common (*e.g.* in 30 to 40%) after 80 Gy from radioiodine, but considerably less frequent after 40 Gy.

Evidence of impairment of thyroid reserve without substantial decrease of thyroid hormone level or normal function has recently been obtained in four subjects whose glands are estimated to have received about 3 Gy, largely from radioiodine in fallout. Other people exposed to thyroid doses of about 10 Gy at the same time have been found to have minor elevations of blood concentration of thyroid stimulating hormone. It remains uncertain whether any deficiency in thyroid function will develop in any of these cases.

Impairment of the normal function of other human endocrine glands has been observed following doses of some tens of grays delivered during radiotherapy. Impaired adrenal reserve, as indicated by a reduced hormone output after pituitary hormone stimulation, was seen after doses of over 30 Gy but not at doses below 20 Gy. A decreased output of various anterior pituitary hormones after appropriate stimulation of this gland has been seen after doses of over 25 Gy in childhood, and clinical evidence of hypofunction at doses over 50 Gy. Tissue necrosis of the anterior pituitary follows doses of some hundreds of grays. There is some evidence that the hypothalamus is more sensitive than the anterior pituitary.

There is little indication of the sensitivity of the pancreas or of the posterior pituitary. The increase in parathyroid activity sometimes observed after irradiation of these glands appears to be due to benign tumour induction and so is presumably stochastic.

Proceedings of the MRC Committee on Protection against Ionizing Radiations

NON-STOCHASTIC EFFECTS OF RADIONUCLIDES

By M. F. Cottrall

Royal Free Hospital School of Medicine,
Pond Street, London NW3

Non-stochastic effects in man have been reported following accidental, occupational and therapeutic exposure to the radiations from a variety of internally deposited radionuclides. Experiments on animals have provided additional evidence as to the nature and magnitude of the effects on individual tissues. The data available were summarized in a table showing the threshold radiation doses reported to produce a given effect.

It was emphasized that the dose/effect relationships were expressed in a variety of ways, and were complicated by the spatial and temporal distributions of dose arising in individual circumstances. Radionuclides emitting α particles and Auger electrons could sometimes produce similar microdistributions of dose in radiosensitive regions resulting in RBE factors considerably in excess of unity. To relate the effects produced by radionuclides possessing widely different residence times in tissues, an attempt had been made to use the NSD concept, but dose rates were generally less than 10 cGy (rad)/h and the validity of the concept under these conditions had to be established. Radionuclides such as ^{65}Zn were incorporated into vital molecules such as hormones and enzymes. Radiation damage to these might produce systemic effects such as changes in autoimmunity which would result in tissue reactions largely unrelated to the radiation dose delivered.

It was concluded that the non-stochastic effects of radionuclides are usually consistent with those expected from the effects induced by external X irradiation. However, radiographic lesions produced in bone by ^{226}Ra, functional loss of thyroid tissue due to radioisotopes of iodine, the effects of ^{239}Pu in the eye and the systemic effects of ^{65}Zn warrant further study. The ovary might also be especially sensitive to the protracted irradiation arising from the presence of certain radionuclides.

COMMENTARY ON THE DISCUSSION

By K. F. Baverstock

MRC Radiobiology Unit, Harwell, Oxon

Meaning of term "non-stochastic"

Most speakers touched upon the question of what was meant by the term "non-stochastic" and questioned the usefulness of the term.

A stochastic consequence of radiation may be defined as one whose frequency of incidence rather than its severity is related to dose without any threshold. A non-stochastic consequence is therefore one whose severity is related to dose but for which there may be a threshold below which either effects do not occur or are of no consequence.

Dr. Field preferred to refer to tissue damage rather than use the term non-stochastic but acknowledged the inherent difficulty of defining what should constitute a threshold since the sensitivity with which tissue damage could be detected depended upon the technique applied to detect it. Dr. Denekamp suggested that the threshold of importance in radiological protection was lack of organ function. However, for organs with slowly proliferating cells the time delay between irradiation and the manifestation of lack of function may be many months or even years. Dr. Mole suggested that stochastic effects may be termed haplocytic—*i.e.* effects derived from changes to only one cell, whereas non-stochastic effects may be termed polycytic—*i.e.* involving many cells. Dr. Field thought that the understanding of the cellular mechanisms by which these various effects arose was an insufficiently secure base on which to build terminology. It was preferable to describe the effects rather than to assume the mechanisms which lay behind the effects.

Extrapolation from animal to man

Dr. Lyon illustrated some of the problems of using experimental animal data to deduce effects in man. Experiments with mice and guinea pigs showed quite different sensitivities of cells in the gonads. The human male was thought to be even more sensitive. Also evident from animal studies were significant differences from one individual to another.

Latent effects in irradiated organs

Sir Edward Pochin drew attention to effects particularly in thyroid which affect an organ's ability to respond to a challenge whilst leaving it apparently unimpaired in the resting state. Similarly, Professor Lajtha drew attention to residual damage in the haemopoietic system. After a sufficiently large proportion of bone marrow cells had been killed by irradiation their ability to repopulate after subsequent challenges was reduced.

Quantification of effects

The organs most at risk from non-stochastic effects were clearly the human testis and ovary. However, the dose limits to these organs are controlled by stochastic considerations, namely hereditary effects, and the non-stochastic limits are not reached in practice.

Other organs which showed effects of dose of the same order of magnitude as the non-stochastic limit were lens of the eye, thyroid and bone. The skin, which has traditionally been a limiting factor in occupational contexts, was thought to be sufficiently protected by the 500 mSv (50 rem) limit. The latest recommendation of ICRP accepted that 20 Sv delivered over weeks or months to limited areas of skin may give rise to cosmetic effects. It was suggested that even greater sparing would result if dose was fractionated over longer periods.

The lens of the eye needed careful consideration. The lowest threshold for opacification which can be detected, *i.e.* as microscopic opaque spots in the lens, need not impair the organ's function. However, in view of the possible lack of clearance of cellular debris from the lens, any effect could be cumulative. It was understood that an ICRP task group would shortly report on this matter.

Concern was expressed that the thyroid was given insufficient attention by ICRP. Dr. Malone said that effects such as nodule growth and cancers which were surgically treatable and therefore not fatal were not given sufficient weight in calculating dose limits. It would not be desirable to allow doses that gave rise, with a probability of unity, to effects which while not fatal needed surgical or other treatment. The problem could be overcome by creating a third category of hazard, namely non-fatal effects requiring medical treatment.

Bone was an organ for which there was evidence that the young were prone to stunting of growth by relatively small doses. Dr. Mole suggested that for this organ, and for the CNS for which there was also evidence of a similar nature, the effects over a life-time were unlikely to be serious.

Social aspects

The decision of how much weight should be attached to a particular hazard was essentially a social one. For example, how should the non-fatal cancers be treated in comparison to the fatal ones? At the moment they were given little weight. Sir Edward Pochin pointed out that on any weighting of years of life lost, either due to death or as impaired quality of life due to necessary treatment, fatal cancer would be of overwhelming importance. He acknowledged, however, that there may be other social considerations. He denied that frequency of thyroid nodule induction would approach unity with the present non-stochastic limit but agreed that the philosophy of ICRP would be severely undermined should any deleterious effect requiring treatment be limited in such a way that it approached a frequency of unity. He did not agree to Dr. Malone's suggestion for a third separate category of damage.

Internal emitters

Dr. Cottrall showed that there was little or no firm evidence in the literature that the effects of internal emitters were more serious dose for dose at a given quality than external radiation. He did, however, note that relatively small doses from about 0·1 μg ^{226}Ra in the skeleton had caused radiographic lesions (small rarefactions observable in X-ray pictures) in man. Professor Spiers pointed out that the mean dose to marrow from 0.1μg ^{226}Ra maintained for 50 years in the bone of an adult man would be about 5–10 cGy (rad). For the fraction of marrow within α-ray range the dose would be 3–4 times greater and for soft tissue inclusions within bone itself about 10 times greater still. A quality factor of 20 would apply to all these doses.

Proceedings of The British Institute of Radiology

Thirty-eighth Annual Congress, April 17–18, 1980

Isotopes in oncology

The following abstract was inadvertently omitted from the Proceedings published in THE BRITISH JOURNAL OF RADIOLOGY, *53* 1114–16 (November 1980). We apologize for any inconvenience caused.

TUMOUR LOCALIZATION WITH GALLIUM-67 AND INDIUM-111 RADIOPHARMACEUTICALS

By D. M. Taylor

University of Heidelberg and Kernforschungszentrum Karlsruhe, Institut für Genetik und für Toxikologie von Spaltstoffen, Postfach 3640 D 7500 Karlsruhe 1, Federal Republic of Germany

^{67}Ga citrate and ^{111}In-Bleomycin have been in clinical use for more than a decade. Neither of these radiopharmaceuticals are tumour-specific and uptake occurs in all normal tissues and in many sites of infection.

Both agents concentrate to some extent in a wide range of tumours, but the uptake may be quite variable in tumours of the same histological class, both between different patients and between different tumour sites within the same patient.

In general ^{111}In-Bleomycin is no better, or is inferior to ^{67}Ga citrate for tumour visualization, except perhaps for the visualization of abdominal lesions. ^{67}Ga, and to a lesser extent ^{111}In, are useful in establishing a differential diagnosis, particularly in the chest and in the differentiation between seminoma and teratoma. ^{67}Ga is also useful in delineating the total extent of malignant disease especially around the mediastinum, where neither X rays nor CAT scans provide good information, and in the staging of Hodgkin's disease and the lymphomas.

They cannot however provide a primary diagnostic screen. The physiological mechanisms underlying the uptake of gallium and indium by tumours are still incompletely understood. Their uptake appears to be directly related to lysosomal enzyme activity in tumours and normal tissues and other important factors are plasma and lysosomal membrane permeability and transferrin.

Rapidly growing tissues tend to show both increased cell permeability and lysosomal activity compared to slowly growing or resting tissues. Thus a "^{67}Ga-avid tumour" is probably more "active" than a tumour showing only weak ^{67}Ga uptake. Radiation or chemotherapy which retards or inhibits tumour growth also reduces ^{67}Ga uptake. This reduction of loss of ^{67}Ga concentrating ability by a tumour, measured by serial quantitative scans, may provide a useful index of the response of the tumour to treatment and of prognosis.

Since the accumulation of ^{67}Ga citrate or ^{111}In-Bleomycin by a tumour is a dynamic process, these two expensive radiopharmaceuticals can be exploited to yield useful functional information about the tumour, in addition to a static image of the tumour distribution, and this should be the major objective of future studies with these two radionuclides.

Forthcoming events

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

The Role of Radiology in the Management of Jaundice

Joint meeting with the Royal Society of Medicine (Section of Radiology) and the Royal College of Radiologists, to be held at the RSM, Wigmore Street, London W1, on Friday January 16 at 5.30 p.m. Speakers will be Dr. L. Kreel, Dr. L. A. Berger and Dr. A. Hilson. It will be followed at 7.30 p.m. by the RSM's Finzi Lecture, by Professor H. J. Burhenne of the University of British Columbia, on "Conventional and interventional radiology for the management of jaundice".

Advanced Educational Seminar Diagnostic Ultrasound

January 26–30, 1981. This programme is designed to offer the practising sonographer or sonologist a review of current concepts in abdominal, obstetrical, and gynaecological ultrasound, as well as discussions on new applications of the modality. Each participant will be provided with approximately 30 hours of formal instruction through lectures, film reading sessions, panel discussions, and practical demonstration. Each participant should plan on bringing a variety of clinical cases for display and discussion by the group. Enrolment for this programme will be limited to 50 participants.

Faculty: Dr. E. A. Lyons and Dr. R. E. Brown (Associate Professors of Radiology, University of Manitoba), Dr. M. L. Johnson (Associate Professor Medicine and Radiology, University of Colorado), Dr. F. Kremkau (Associate Professor of Medicine (Biophysics) Winston-Salem, North Carolina), Dr. F. Manning (Associate Professor of Obstetrics and Gynecology, University of Manitoba), Dr. C. Merritt (Chairman of Radiology, New Orleans, Louisiana), and Dr. David Tubman (Assistant Professor of Radiology, University of Manitoba).

For further information please contact: Advanced Educational Program, Department of Diagnostic Ultrasound, Health Sciences Centre, 700 William Avenue, Winnipeg, Manitoba R3E 0Z3, Canada. Telephone: 1-204-787-3701.

Medical Ultrasonic Images: Formation, Display and Recording

The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB), in association with Polaroid Corp., announce a symposium to be held January 31–February 1, 1981, at the Hilton Hotel, Brussels. The programme will include papers and discussion on the physiology of image perception, transmission and display of image information and various facets of image formation, analysis and enhancement. Image artefacts and their elimination and properties of cathode-ray displays will also be covered. Presentations will be given on the primary recording processes as well as an assessment of recording media.

For further information and registration forms, please contact EFSUMB, c/o Burson-Marsteller, Box 5, Avenue Louise 225, Brussels, Belgium.

Radioisotopes in Gastroenterology

An all-day meeting, organized by the BIR Nuclear Medicine Committee and starting at 9.30 a.m., will be held on Wednesday, February 18 at the Institute House, 32 Welbeck Street, London W1. Proffered papers on gastric emptying, bile acid metabolism, hepatobiliary scintigraphy, absorption studies, etc., should be sent to Dr. M. V. Merrick, Western General Hospital, Edinburgh EH4 2XU before December 31.

Silvanus Thompson Memorial Lecture

Will be held at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG on February 18, 1981, the speaker to be Professor J. R. Mallard. For further information contact the General Secretary.

Radionuclides in Gastroenterology

A meeting to be held on February 18, 1981 organized by the Nuclear Medicine Committee of The British Institute of Radiology, at Institute House, 32 Welbeck Street, London W1M 7PG (01–935 6237). Further information from the General Secretary.

State of the Art Seminar: Management of Metastatic Malignancy—Can Adult Oncology Learn from the Paediatric Field?

A meeting to be chaired by Dr. Dorothy Pearson will be held at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, on February 19, 1981. For further information contact the General Secretary.

Combined Radiotherapy and Chemotherapy: Advantages, Disadvantages—Can Radiobiology Help?

An evening meeting to be held on February 19, 1981, organized jointly with the Royal Society of Medicine (Section of Radiology) and The Royal College of Radiologists. Speakers: Drs. D. P. Deakin, J. Moore, Dorothy Pearson and Ruth Sandiland, 32 Welbeck Street, London W1.

BIR Radiobiology Meeting

There will be a general radiobiology Work-in-Progress meeting at 11.00 in the Institute on February 20, 1981.

First Annual Banff Radiology Seminar

Banff Springs Hotel, Canada, February 22–27, 1981. Guest faculty includes John A. Campbell, M.D., James A. Christie, M.D., Charles R. Drew, M.D., John L. Gwinn, M.D., Patrick F. Sheedy, M.D. and Hooshang Kangarloo, M.D. For further information write to Richard L. Wesenberg, M.D., Director of Radiology, Alberta Children's Hospital, Calgary, Alberta, Canada T2T 5C7.

Symposium on Colorectal Cancer

To be held on February 27–28, 1981 at Jarvis Hall, 66 Portland Place, London W1. A multi-disciplinary symposium organized by The Royal College of Radiologists and intended for consultants, senior registrars and research workers, but open to all interested medical practitioners. Registration fee £25·00. Full details from The Meetings Secretary, RCR, 38 Portland Place, London W1N 3DG.

Radiographic Systems: What is Best?

An all day meeting is to be held at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG on March 18, 1981. Speakers: Prof. B. R. Pullan, Drs. G. M. Ardran, J. H. E. Carmichael, D. H. Trapnell and G. R. Higson. For further information contact the General Secretary.

Forthcoming events

Spring Meeting, BIR/RCR/RSM

A joint Spring Meeting, organized by The Royal College of Radiologists, will be held in Bristol on April 3–4, 1981. For further information contact the General Secretary, The Royal College of Radiologists, 38 Portland Place, London W1.

British Nuclear Medicine Society
Annual Scientific Meeting, 1981

The British Nuclear Medicine Society will be holding its 9th Annual Scientific Meeting on April 6, 7 and 8, 1981 at Imperial College, London. The closing date for abstracts is January 24 and forms can be obtained from the Conference Secretary at 22 Leinster Avenue, East Sheen, London SW14 7JP.

BIR Annual Congress 1981 and Scientific Exhibition

The British Institute of Radiology Annual Congress will be held on April 9–10, 1981 at the Royal Free Hospital and will include the Mackenzie Davidson Memorial Lecture by R. G. Grainger on "Intravascular contrast media—present perspectives". Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

Physics in Medical Ultrasound
Durham, April 13–14, 1981

This meeting, organized by the HPA Ultrasonics Topic Group in association with the British Medical Ultrasound Society, is intended to provide a forum for the presentation and discussion of scientific and technical aspects of ultrasound in medicine, and will be accompanied by an exhibition of commercial test and research equipment. Accommodation available. Offers of papers, particularly under the headings: Quantitative assessment of equipment; New techniques and developments; and Physics of imaging, to Dr. T. A. Whittingham, Regional Medical Physics Department, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE.

Echocardiography

A course in Echocardiography will be held are Harefield Hospital from April 27 to May 1, 1981. The course is intended for those having experience in cardiac ultrasound and working in the field. Accommodation available. Further details from Mrs. M. Beech, telephone Harefield 3737, ext. 609.

Fourth European Congress on Ultrasonics in Medicine

This will be held in Dubrovnik, May 17–24, 1981, sponsored by EFSUMB and organized by the Yugoslav Association of Societies for Ultrasound in Medicine and Biology. Information from Dr. Višnja Latin, M.D., D.Sc., President of the Organizing Committee, Jagode Truhelke, 26, 41090 Zagreb, Yugoslavia.

Fifth Congress of the European Nuclear Medicine Society
Nineteenth Congress of the Societa Italiana di Biologia e Medicina Nucleare

Pisa, June 9–12, 1981. Main suggested topics: cardiovascular applications of radionuclides *in vivo* and *in vitro*; advances in regional lung morphofunctional studies; development of radioimmunoassay in comparison with non-radioactive immunochemical techniques; advances in nuclear imaging in comparison with alternative techniques. Official language: English. There will also be an industrial and technical exhibition.

Registration forms and other information from: The Organizing Secretariat, OIC, Via G. Modena 19, 50121 Florence, Italy. (Registration by April 15, 1981).

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Programme from: ICR81, c/o Brussels International Trade Fair, Parc des Expositions B-1020, Brussels, Belgium.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

Workshop on Research Concerning Toxicity of Contrast Materials in Radiology

September 17–18, 1981, in Lyon. For information please write to Prof. M. Amiel, "Séminaire Produits de Contraste", Hôpital Cardiologique, B.P. Lyon Montchat, 69394 Lyon Cedex 3, France.

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

The Neutron and its Applications

The Institute of Physics, in collaboration with AERE Harwell, is organizing an international conference in Cambridge, September 13–17, 1982, to mark the 50th anniversary of the discovery of the neutron.

The conference aims to cover all aspects of neutron science. Plenary lectures will include G. Allen on the contribution of neutron scattering to the understanding of macromolecules, J. F. Fowler on neutrons in medicine, A. M. Lane on nuclear reactions caused by neutrons, C. Llewellyn-Smith on the structure of the neutron, A. R. Mackintosh on the contribution of neutron scattering to the understanding of magnetism, N. F. Ramsay on particle properties of the neutron, and C. G. Schull on wave properties of the neutron. The conference will include a commemorative session and a public session devoted to issues of general concern. There will be exhibitions of scientific equipment, and of historical interest.

Further information from the Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.

Book reviews

Review of Gross Anatomy By Ben Pansky. 4th edit., pp. xiii + 524, illus., 1979 (Macmillan Publishing Co., New York; Collier Macmillan Canada, Ltd., Toronto; Bailliere Tindall, London), £9·50.
ISBN 0–02–390630–8

This compact volume published in soft covers consists essentially of a series of line diagrams with accompanying synopses of regional anatomy. In addition there are a number of photographs of surface anatomy, bones and selected radiographs. The drawings are the work of the author and depict the points of anatomical importance both clearly and elegantly. Most are in black and white although colour has been added to a few for greater impact. All are beautifully annotated to furnish an immediate reminder of the salient anatomical features of each region. The book thus provides an attractive, efficient and convenient vehicle for the revision of regional anatomy. It is not aimed particularly at the radiologist and does not contain illustrations of cross-sectional anatomy which has become so important following the introduction of ultrasound and CT investigations.

The author in his preface, wisely reflects that anatomy "once learned and quickly memorized, is just as easily forgotten". He has presented the essential facts in a format which facilitates effective and rapid revision. Students for the first examination of the F.R.C.R. and their instructors will find this book invaluable. It can be thoroughly recommended for inclusion in the libraries of all teaching units.

J. Roylance.

Catalogue of Spectral Data for Diagnostic X rays. By R. Birch, M. Marshall and G. M. Ardran. pp. 142, 1979. HPA Scientific Report Series 30 (Hospital Physicists' Association, London), £9·50.
ISBN 0–904181–13–8

For many investigations in diagnostic radiology, knowledge of the X-ray spectra used is of importance. With the increasing availability of semiconductor detectors, in conjunction with multichannel analysers, an increasing number of measured spectra have been published. There are, however, a number of severe experimental problems, *e.g.*:

(i) even at extended focus detector distances (several metres) and with very narrow collimators (<1 mm diam.) the exposure rates under normal operating conditions of diagnostic X-ray tubes are much too high for the extremely sensitive semiconductor spectrometers. On most generators the waveform and therefore the spectrum depends on the tube current—reducing the tube current to get acceptable count rates may therefore lead to erroneous results;

(ii) the difficulty of investigating the effect of the target angle is obvious.

An alternative is to calculate the X-ray spectra. The authors found that none of the theoretical models fitted their measurements with the desired accuracy. So one of the parameters was determined empirically by fitting measured low-current, constant-potential spectra in the range 30–150 kV. The authors also calculated several spectra according to the reviewer's specifications, with very good agreement with his measured data. This gives confidence that the calculated spectra are also valid for conditions where the spectra cannot be measured.

Apart from a short introduction to the subject, and a section on derivation and presentation of the data, the catalogue contains data on a large variety of X-ray spectra. One page is devoted to each spectrum. Photon spectra are given both in graphical (normalized to the peak channel) and tabular form (normalized to a total of 10^5 counts). The total photon flux at 75 cm is also given, together with the mean photon energy. Also plotted are relative kerma spectra in air. From this are calculated the mean energy, output in Gy/mAs and exposure, as well as the first three half-value layers in aluminium. For people accustomed to film penetrameters the penetrameter estimates of voltage and filtration may be useful.

The section on constant-potential generators contains 31 spectra in the range 50–150 kV with total filtrations from 1.5 to 4 mm Al and 0.25 mm Cu; further included are 12 mammographic spectra from tungsten and molybdenum tubes at voltages from 30 to 50 kV, as well as eight spectra for different CT scanners. The effect of voltage ripple is demonstrated in three spectra from six-peak generators and seven spectra from two-peak generators. There are seven photon spectra comparing different target angles. Based on nine incident spectra, 34 transmitted spectra through varying thicknesses of tissue, bone plus tissue, and Ca plus tissue are reproduced. In the final section the absorption characteristics of a large selection of commercially available intensifying screens are given.

Whereas the photon spectra and half-value layers agree very well with measured data (where available), the predicted exposure rates are always higher than experimental data, on average by 32%; this has been accounted for with all exposure rates quoted for the spectra. For the calculation of the kerma spectra the mass-energy absorption coefficients given by ICRU have been used; Hubbell had found differences up to 8% in the energy range 20–50 keV. As both these points are discussed in the catalogue this should not lead to misunderstandings.

Conclusion: The catalogue contains a large number of calculated diagnostic spectra under normal operating conditions where measurements are rather difficult if not impossible. Where measured data exist, both from the authors and the reviewer, the agreement is excellent. The catalogue should therefore prove most useful as a collection of basic data for all researchers interested in the physics of diagnostic radiology.

W. W. Seelentag.

Gastrointestinal Radiology. A functional approach to radiological investigation and diagnosis. By Marcel M. Brombart. pp. viii + 452, 1980 (Georg Thieme, Stuttgart), DM248.
ISBN 3–13–5749–010

For over 30 years Dr. Brombart has been interested in gastrointestinal radiology. In this beautifully produced book he presents the reader with the fruits of the experience he has gained in that time. It is obvious from the introduction that this book is the work of an enthusiast willing to allow that newer methods such as angiography and double contrast examination have a place in the radiologist's armamentarium but that their place is a supplemental one and that the ultimate diagnosis will in the majority of cases depend on careful fluoroscopy and the obtaining of appropriate films. This book of approximately 450 pages and over 1700 X rays and line drawings certainly presents a strong and cogent argument in support of this view. The author approaches the gastrointestinal tract not in the conventional organ-by-organ fashion but in the highly practical way of discussing specific pathological entities and syndromes. Each chapter contains a short introductory section on pathology followed by a very full discussion of the radiologic features with appropriate X rays and line drawings.

This book is certainly one that should be read by all who are interested in gastroenterology and clearly demonstrates the continued place of careful fluoroscopy in diagnosis.

J. A. Gleeson.

Application of the Dose Limitation System for Radiation Protection. Practical Implications. Proceedings of a Seminar, Vienna, 5–9 March, 1979, pp.xvi+674, 1979 (International Atomic Energy Agency, Vienna), Aust.sch. 970.
ISBN 92-0-020379-5

This seminar was held following the issue of ICRP Publication 26 in 1977, which established a system of dose limitation to enable assessment to be made of the justification for practices involving the exposure of people to radiation, and the enunciation of the principle that all exposures to radiation should be as low as readily achievable (ALARA), economic and social factors being taken into account. It enabled a group of over 200 experts from 35 countries and several international organizations to hear and discuss 42 papers in eight sessions and to participate in panel discussions of radiation risk assessment and optimisation of radiation protection. The papers are printed as submitted by their authors, and discussions are reported in some detail.

A wide range of topics is covered within the general theme, and most authors are acknowledged world experts in their fields. The early papers generally look at the ICRP recommendations and their underlying philosophy, while later papers in five sessions are devoted to practical aspects of their application, predominantly in relation to the exposure of workers and the public at large. Several papers relate to their implementation in particular countries (*e.g.* UK, USSR, Israel) or work (*e.g.* nuclear medicine, uranium mines).

Some papers would be of particular interest to readers of this Journal in addition to the introductory papers. One is "Optimization of radiation protection" by D. Beninson (although he refers to cost in US dollars per man-rem) who suggests ways of balancing the cash cost of additional radiation protection measures against the cost of not carrying these out, assessed in terms of the probability of resulting death. This idea is pursued further in relation to afterloading in brachytherapy in a paper from Denmark ("The monetary value of the man-rem and optimization in radiation therapy (brachytherapy)" by K. R. Ennow and K. A. Jessen). Their conclusion is that the expense of installing afterloading solely to protect staff from radiation would be unjustified in terms of the expected reduction in exposures, but could be justified if it resulted in substantial reduction of clinical complications caused by radiation damage to rectum and bladder. Several papers (*e.g.* those by Lafontaine of Belgium, Zerbib of France and Weiler-Madsen of Denmark) discuss ICRP Publication 26 from the point of view of the radiation worker and his medical surveillance.

This volume is one that will find a place in reference libraries and on the shelves of those concerned with the broad policy of radiation protection, its philosophy and its implementation in general terms. It will not be of much use to the average radiological protection adviser or radiation safety officer. It inevitably suffers from the defects of most reports of such seminars in that it reflects the special interests of the participants without quite managing to cover the subject as a whole. There is little mention of radiation protection in medicine and hardly even a passing reference to diagnostic radiology (which contributes a large fraction of all man-made radiation to which the public is exposed in industrialized countries), apart from one paper from Sweden entitled "Significance of photon attenuation for the choice of quantities in X-ray protection" by L. G. Bengtsson and M. Jensen. There is nothing at all to suggest how developing countries justifiably planning to extend their radiological facilities could take the dose limitation system and optimization into account in doing so. Perhaps it is intended that this will be the subject of a future seminar.

S. B. OSBORN.

Glucagon in Gastroenterology. Edited by J. Picazo. pp. 146, illus., 1979 (M.T.P. Press Limited, Lancaster, England; Novo Research Institute, Bagsvaerd, Denmark), £2·45.
ISBN 0-85200-254-8

This book is the result of an International Workshop on "Glucagon in Gastroenterology" held in Madrid in May, 1978. The papers presented are published together with edited versions of the discussions which followed each presentation.

One chapter, 25 pages in length (including illustrations, extensive references and discussion), written by Dr. L. Kreel, is devoted to radiology. It stresses the smooth muscle relaxant effect and possible radiological uses of glucagon in all systems but especially in the gastrointestinal tract with emphasis on the importance of this in conjunction with double contrast examinations. Unfortunately the claim that lesions such as gastric erosions, polyps, ulcer scars and early gastric cancer are better visualized, is not helped by disappointing illustrations and where the films demonstrating the duodenum are either in single contrast or taken during a peristaltic wave. The illustration of the oesophagus, though elegant, is unnecessary as glucagon does not inhibit oesophageal peristalsis.

Dr Kreel has written an extensive review article including the same subject in this Journal in September, 1975. This chapter does not add significantly to that review. This book will be a useful addition to gastroenterological units for its succinct and eminently readable presentation of the multiple uses of glucagon in the pararadiological aspects of the gastrointestinal tract.

J. VIRJEE.

Radiographic Atlas of Colon Disease. Ed. E. I. Greenbaum, pp. 664, 1980 (Year Book Medical Publishers, Chicago and London), £18·00.
ISBN 0-8151-3923-3

When I tell you that there are 62 (mainly American) authors and over 2000 illustrations you will know what sort of book to expect—comprehensive and authoritative. You will not be disappointed. There are 49 chapters, each dealing with some aspect of colonic disease or technique of examination. The format chosen for each chapter is a few pages of text with references followed by a collection of pictures. Editorial discipline is excellent with a crisp presentation of facts. The multiplicity of authors does not jar. The quality of reproduction of the figures is satisfactory. Perhaps to the surprise of British readers, in the illustrations single contrast films outnumber double contrast examinations.

Each disease is dealt with in turn, in alphabetical order, from "abnormalities of haustration" and "amebiasis" [*sic*] to "villous adenoma" and volvulus". This arrangement has disadvantages. For instance, the inflammatory diseases are scattered throughout the book, and if you want to know the causes of a mucosal disease of the rectum or a stricture of the sigmoid you have to search through the entire book. A chapter on the radiological distinction between the various forms of colitis would have been worthwhile. I would have liked more emphasis on what is a major problem in day to day colonic radiology—distinguishing between a normal and slightly abnormal bowel. Nearly all the examples of disease shown are florid and well established.

This is the only English-language book devoted to radiology of the colon and it fills the gap admirably. It should be in departmental libraries. By modern-day standards it is cheap.

J. G. B. RUSSELL.

Instructions to authors

Please keep manuscripts brief and concise and include only those illustrations essential to an understanding of the text.

Much time and correspondence will be saved if authors pay careful attention to these detailed instructions.

Material published in THE BRITISH JOURNAL OF RADIOLOGY includes full papers, case reports, technical and instrumental notes, short communications, letters to the editor and invited articles. Communications should ordinarily be addressed to the Honorary Editors, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Communications from North America, Continental Europe, Australasia or South Africa should preferably be submitted to the most appropriate of the following Associate Editors:

Dr. P. Armstrong, M.B., B.S., F.R.C.R., D.M.R.D., Department of Radiology, School of Medicine, University of Virginia, Charlottesville, Virginia 22901, USA (for diagnostic papers).

Prof. M. Cohen, Department of Physics, Montreal General Hospital, 1650 Cedar Avenue, Montreal, H39 1A4, Canada (for non-diagnostic papers).

Prof. B. J. Cremin, F.R.A.C.R., F.R.C.R., Department of Radiology, Red Cross Children's Hospital, Rondebosch, Cape Town 7700, South Africa.

Dr. H. A. Luke, F.R.C.R., F.R.A.C.R., The Alfred Hospital, Prahran, 3181, Victoria, Australia (for diagnostic papers).

Dr. G. P. G. Sim, M.B., F.R.C.R., M.R.C.A., X-ray Department, Wellington Hospital, Wellington, New Zealand.

Dr. R. Fox, D.Phil., Department of Medical Physics, Royal Perth Hospital, Perth, Western Australia (for non-diagnostic papers).

Prof. D. M. Taylor, Institute for Genetics and for Toxicology of Fissile Materials, Kernforschungszentrum, Postfach 3640, D–75, Karlsruhe J, Germany.

The acceptance of a paper for publication in THE BRITISH JOURNAL OF RADIOLOGY is at the discretion of the Editors and is subject to the understanding that the material contained in the paper has not already been published and is not intended for publication elsewhere.

If a paper has more than one author, the negotiating author is expected to bear responsibility for obtaining the agreement of all the other authors.

The copyright of all publications resides with The British Institute of Radiology.

The Editors take no responsibility for the return of MSS, prints, etc. submitted for publication.

MANUSCRIPT. The manuscript should be typewritten in English on one side of the paper only with double spacing and margins of at least 25 mm on both sides and at the top. The top copy must be submitted together with one duplicate. The address given in the title should be that of the department(s) or hospital(s) at which the work was carried out. If any author has subsequently moved to a new address, this should be given as a footnote. Degrees and diplomas of authors should be given but not more than three for each author. Tables (numbered I, II, etc.) should be given on separate sheets, and each should have a short descriptive title. Legends for illustrations, including diagrams and graphs, should be set out on a separate sheet, and denoted Fig. 1, 2, etc. The initial letter of trade or proprietary names should be a capital. Mathematical expressions should be set out very clearly. Paragraphs should be indented.

UNITS, SYMBOLS AND ABBREVIATIONS

Authors should use the *International System of Units (SI)* (B.S.I., 1970; WHO, 1975). The publication *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (Royal Society of Medicine, 1977) is thoughtful and critical on this subject; authors are strongly recommended to follow the detailed suggestions in this guide and to note particularly the comments made on the choice of units. Units of radiation should be given in SI with the old units in parentheses, thus 1Sv (100 rem), 200 cGy (rad), 1 MBq (27 μCi). Some explanation and a table of conversions appeared in an Editorial, Vol. 52, page 1, 1979.

DIAGRAMS AND GRAPHS. Diagrams and graphs, including numerals and lettering, should be clearly drawn in black ink for photographic reproduction to a width of 76 mm (exceptionally 156 mm). Good quality photographic prints or the original art work should be supplied. Care should be taken that details such as numbering and experimental points remain legible after photographic reduction. Computer print-outs are seldom satisfactory. The figure number, author's name and title of article should be pencilled lightly on the back of each illustration.

Authors of physics papers will find advice on drawing diagrams, particularly electrical circuits, in *Notes for Authors* issued by the Institute of Physics and the Physical Society in 1976.

RADIOGRAPHS. Unmounted prints not larger than whole plate, 216×152 mm, and not smaller than half plate should be supplied with MSS; if the prints are not of sufficiently high standard for reproduction purposes the author will be required to submit the original radiographs and to defray the cost of making prints. Tracings of sections of prints are acceptable when necessary for additional clarification. Hospital illustrators and photographers are usually familiar with the style of drawing or print which will give the best reproduction.

COLOUR. Drawings or photographs in colour are very expensive and are acceptable only if the author is prepared to pay the additional cost of block-making and printing.

REFERENCES. The Harvard system is used. In the text these should consist of the names of authors and the year of publication. When there are more than two authors only the first followed by *et al.* should be used. In the bibliography references will be given *in full* and will include the title of the paper and the full name of the journal or other publication in which the article cited appeared. Both first and last page numbers are required. The references must be arranged in alphabetical order, in the following form:

Examples

Brownell, G. L., Aronow, S. and Hine, G. J., 1976. Radioisotope scanning. In *Instrumentation in Nuclear Medicine*, Ed. G. J. Hine, Vol. 1 (Academic Press, New York), pp. 381–428.

Watson, A., Russell, J. G. B. and Torrance, G. B., 1970. Hepatic blood flow and Biligrafin excretion during intravenous cholangiography. *British Journal of Radiology*, *43*, 248–250.

All references must appear both in the text and in the bibliography.

ABSTRACTS. Papers (other than case reports and technical notes) should be accompanied by an abstract. This abstract is not part of the paper, but is intended to convey the content of the paper, to draw attention to all new information and to the main conclusions, and should be intelligible in itself without reference to the paper. An abstract should not normally exceed 200 words.

CORRESPONDENCE. Letters for publication in the correspondence section of the journal must be confined to matters of interest to readers of this journal.

SHORT COMMUNICATIONS. These are reports of initial studies in new areas, and comments which are too speculative or provocative for a normal paper. They should be kept as short as possible and must on no account exceed two pages of the journal. They will be published with the minimum delay.

REPRINTS. Twenty-five reprints of each paper are supplied free. Additional copies may be purchased. Reprints of correspondence items will not be supplied unless specifically requested.

SUPPLEMENTS. Special monographs which are too long for publication within the journal, or detailed reports of certain meetings, may be considered for publication as a Supplement.

REFERENCES

British Standard 3763, 1976. *The International System of Units (SI)*, British Standards Institution, London (£6·20).

Institute of Physics, 47 Belgrave Square, London SW1, 1981. *Notes for Authors.*

The Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE, 1977. *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (£2).

Membership Subscription Reminder

Members of The British Institute of Radiology are reminded that new membership subscription rates become due on January 1, 1981, as follows:

Ordinary Member (UK)	£25·00
Ordinary Member (outside UK)	£22·00

Members in training and radiographers pay reduced rates.

Cheques should be made payable to The British Institute of Radiology, crossed and sent to the General Secretary, BIR, 32 Welbeck Street, London W1M 7PG.

Book reviews

An atlas of radiologic anatomy 7
Disorders of the cervical spine 7
L'urographie intraveineuse 17
Dacryocystography 17
Clinical cardiac radiology 23
Therapy and prevention of infections in cancer patients 35
Cancer and the immune response 35
Treatment of radioresistant cancers 60
Atlas of disease and special examination of the breast 77
Differentialdiagnose seltener Lungenerkrankungen im Röntgenbild 77
Review of gross anatomy 87
Catalogue of spectral data for diagnostic X rays 87
Gastrointestinal radiology 87
Application of the dose limitation system for radiation protection 88
Glucagon in gastroenterology 88
Radiographic atlas of colon disease 88

University of Leeds
in association with
The Royal College of Radiologists

THE LEEDS GASTRO ENTEROLOGY COURSE FOR RADIOLOGISTS

will be held at
St. James's University Hospital
Leeds
Monday, 11 May to Friday Noon, 15 May 1981

The Course is designed mainly for Consultants and Senior Registrars who wish to sub-specialize in gastroenterology. It will have a sizeable clinical content and will emphasize special procedures.

The fee for the Course is £80·00 which includes lunches and morning and afternoon refreshments.

Residential accommodation can be arranged if required at a central hotel.

Early application is advised.

Full details together with programme and application form can be obtained from Mr. Frank Moran, Senior Administrative Assistant, Post-graduate Dean's Office, Littlewood Hall, Leeds General Infirmary, Leeds LS1 3EX.

The British Journal of Radiology

TEACHING BOOKLETS

No. 1
The Physical Aspects of Radioisotopic Organ Imaging, by K. G. Leach (1976) £1·50

No. 3
Fundamental Aspects of Medical Thermography, by W. M. Park and B. L. Reece (1976) £3·40

Available from the Publications Office,
The British Institute of Radiology,
32 Welbeck Street, London W1M 7PG

VOL 54 NO 637 JANUARY 1981

The British Journal of Radiology

Contents

Page

Less common stress fractures in the foot. 1
K. O. A. Meurman

Bilateral renal cell carcinoma—unusual occurrence in three members of one family. 8
E. R. Reddy

Aging and simple cysts of the kidney. 12
S. P. Laucks, Jr. and M. S. F. McLlachlan

Lymphograms in prostatic carcinoma: false–positive and false–negative assessments in radiology. 15
T. Sherwood and E. P. N. O'Donoghue

Assessment of progression of secondary bone lesions using serial radionuclide imaging. 18
B. R. Condon, R. Buchanan, N. W. Garvie, D. M. Ackery, J. Fleming, D. Taylor, D. Hawkes and B. A. Goddard

A physical assessment of the imaging performance of a panel-type X-ray image intensifier. 24
G. A. Hay and A. R. Cowen

Radiation myelopathy in patients treated for carcinoma of bronchus using a six fraction regime. 29
S. Dische, W. M. C. Martin and P. Anderson

The relationship of dose to prognosis in squamous-cell carcinoma of the aerodigestive tract. 36
M. Wollin and A. R. Kagan

Interaction of hyperthermia and radiation: radiation quality. 40
D. D. Loshek, J. S. Orr and E. Solomonidis

Technical notes. 48
Angiography assisted by a new videostore system.
R. S. Dossetor, B. Keane, R. D. Jeffrey and J. Pressburger
Factors affecting the breathing rate of mice as used for studies of radiation damage to lungs.
E. L. Travis, J. D. Down, L. Hall, B. Vojnovic and S. J. Holmes
Induced radioactivity in patients from betatron irradiation.
G. W. Bennett, R. Dobert, J. Meltzer, B. E. Archambeau and J. O. Archambeau
In vivo dosimetry in the pelvis during fast neutron therapy.
B. J. Mijnheer, Tj. Wieberdink and J. J. Battermann

Case reports. 61
Achondrogenesis type II in twins.
P. E. Andersen
Pulmonary opacities in pseudoxanthoma elasticum: report of two cases.
H. Mamtora and V. Cope
Chronic recurrent pleural effusion in adult histiocytosis-X.
P. W. Tittel and C. F. Winkler
A case of non-fatal intravasation of barium during barium enema.
F. Holly Archer and A. H. Freeman
Duodenal ulcers causing obstructive jaundice and a mucocele of the gall bladder.
D. C. J. Fernando, T. D. Gopichandran and R. G. Kendrick
Radiation pneumonitis in a patient exposed to asbestos.
R. F. U. Ashford, J. Maher, A. Drury and D. Pickering

Short Communications. 78
Rib artefact in computed tomography.
A. K. Dixon and I. G. Wylie
A comparative trial of three oral cholecystographic contrast media.
A. Cargill and W. Hately

Proceedings of the MRC Committee on Protection against Ionizing Radiations. 81
Radiobiology forum on non-stochastic effects of ionizing radiations, March 4, 1980.

Proceedings of The British Institute of Radiology, Thirty-eighth Annual Congress, April 17–18, 1980. 84
Addendum.

Forthcoming events. 85

Instructions to authors. 89

Printed in Great Britain by Lund Humphries
London and Bradford
Published by The British Institute of Radiology
32 Welbeck Street, London W1M 7PG

ISSN 0007–1285
16011

14.9.82

Vo 54 Number
February 1981

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis
Radiation oncology
Nuclear medicine
Ultrasound
Radiological physics
Radiobiology
Radiation protection
and related disciplines

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01-836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01-935 6237 and 01-935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries

M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

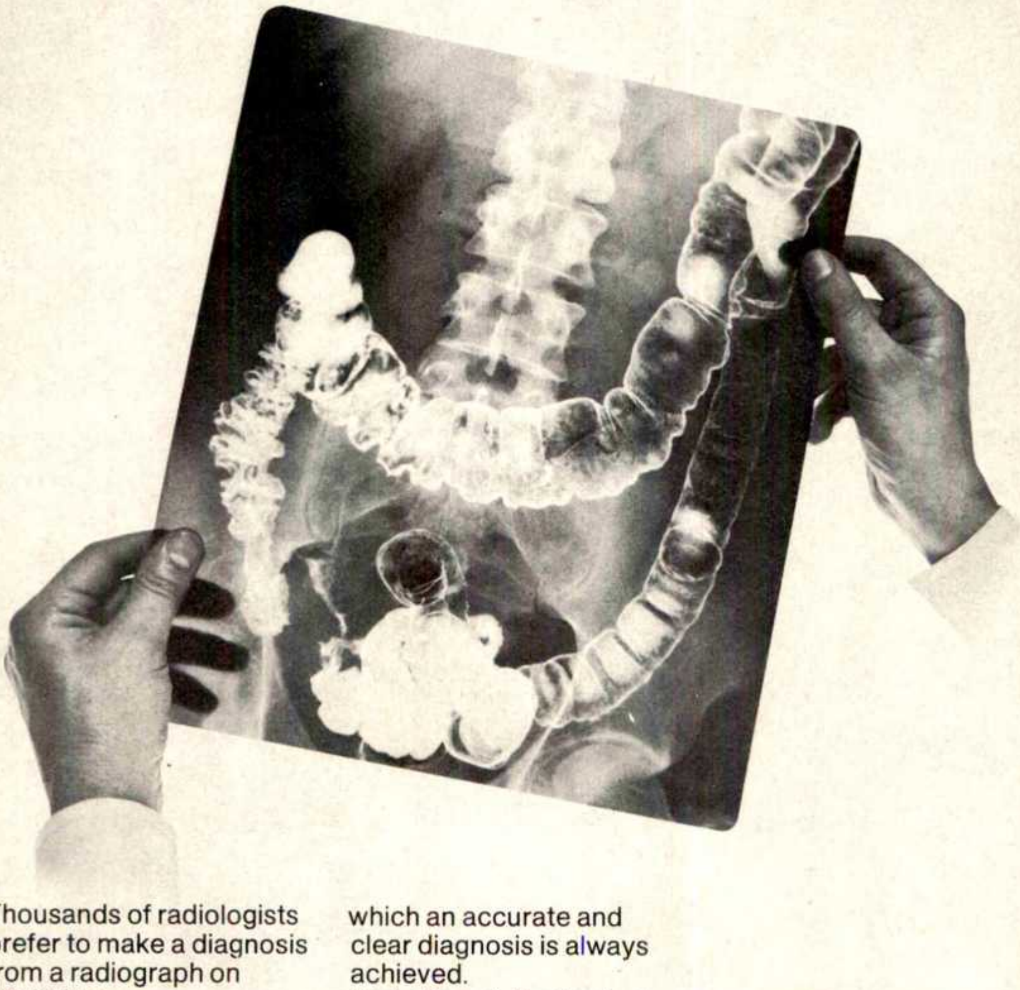
GUERBET INTRODUCES ITS NEWEST CONTRAST MEDIUM. IT ONLY TOOK 10 YEARS OF RESEARCH

hexabrix®
Lower hyperosmola... ...ographic
contrast m...
Monoacid dime... ...acid),
meglumine/sod... ...olution.

GUERBET
Better contrast media through research
LABORATOIRE GUERBET
16-24, rue Jean Chaptal - 93609 Aulnay-sous-Bois - Cedex FRANCE Tel.: 866.78.37 - Telex: 212382 F.

GEVAERT AGFA-GEVAERT

In Europe, every day, more eyes are focused on Curix film than on any other X-ray film.



Thousands of radiologists prefer to make a diagnosis from a radiograph on Curix film.
They are choosing Curix for its high definition, optimum contrast, brilliance and low fog level.
In a word, Curix film means "quality" in medical radiography.
A consistent quality from which an accurate and clear diagnosis is always achieved.
And, after all, that's what really matters.

Further information from:
Agfa-Gevaert Ltd.,
Publicity Department,
Great West Road,
Brentford, Middx. TW8 9AX.
Tel: 01-560 2131.

A system for the 80s that's sure to please........................

Ceiling Tube Support
CH-30X

Features
- Light movement
- Safety
- Convenient, simple operation

The XS-10 features the ease of operation, safety and reliability that only 100 years of SHIMADZU experience in medical engineering can offer.

90°/90° UNIVERSAL DIAGNOSTIC TABLE
XS-10

- 90°/90° table tilting
- Automatic field collimation
- Exposure program up to 14" × 14" (35 cm × 35 cm)
- Cassette loading from either side of spot film device
- Reciprocating X-ray grid in spotfilming
- Built-in bucky device
- 7" image amplifier attachable without ceiling suspension

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan. Phone: Tokyo 03-346-5461 Overseas Telex No. 0232-3291 SHMDT J.
Cable Address: SHIMADZU TOKYO
SHIMADZU (EUROPA) GmbH
4000 Düsseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D

Ontario Cancer Foundation London Clinic

Applications are being invited for a post of Radiation Oncologist in the London Clinic of the Ontario Cancer Foundation. This clinic serves a population of approximately one million people. Between 2,500 and 3,000 new cases of malignant disease are seen each year. It has consultative and follow up clinics in eight cities nearby.

The clinic has its own inpatient beds and outpatient services and ambulant patient accommodation.

The clinic is attached to a general hospital which has modern diagnostic and investigative facilities.

The clinic has five Radiation Oncologists, three Medical Oncologists and three Physicists. The radiotherapy equipment consists of a 33 MeV betatron, a 6 MeV linear accelerator, a telecobalt machine and a 90-kV superficial X-ray machine. Brachytherapy sources include radium needles and tubes and radioactive gold grains. Plans are being made for the purchase of an after-loading apparatus and another 6 MeV linear accelerator.

The successful applicant will be offered an appropriate appointment in the Radiation Oncology Department of the University of Western Ontario dependent upon qualification and experience. The successful appointee will be expected to participate in consultative and follow up clinics. He will also engage in teaching of both undergraduate and postgraduate medical and dental students, and be encouraged to develop his own clinical and/or laboratory research interest. Excellent research facilities exist and the clinic has recently established an active clinical trials unit in London.

Applications with curriculum vitae and the names of three referees should be submitted to
**Dr. H. Bush, Director, London Clinic, Ontario Cancer Foundation, Victoria Hospital,
London, Ontario, Canada N6A 4G5.**

Princess Alexandra Hospital, Brisbane

Full-time Radiologist

Applications are invited from Medical Practitioners with Radiology Specialist Qualifications for the position of full time Specialist Radiologist, Department of Diagnostic Radiology, Princess Alexandra Hospital.

General Information
The Hospital is a major teaching hospital of 1,200 beds associated with the University of Queensland. All specialities except Obstetrics and Paediatrics are represented and the successful applicant would have the opportunity to develop an interest in the Radiology of any of the specialities represented.

The Department of Diagnostic Radiology performs approximately 100,000 examinations including 1,200 procedures per year. Xerography, C.T. Head Scanning, Ultrasonography and Nuclear Medicine facilities are incorporated within the Department.

Remuneration
$34,797 to $42,726 per annum plus call back payments. (This remuneration is made up of salary $32,797 to $40,726 plus an allowance of $2,000 per annum). There is no right of private practice.

Conditions of service include five weeks annual leave, sick leave, conference leave and long service leave.

A very satisfactory superannuation scheme is available. Sabbatical leave is available after 6 years initially and after 4 years thereafter.

Any further information can be obtained by contacting the Director of Diagnostic Radiology, Dr. K. Siddle.

Applications giving details of qualifications, age and experience together with names of three (3) referees should reach the **Medical Superintendent, Princess Alexandra Hospital,
Ipswich Road, Woolloongabba, Brisbane, Queensland (M3464)**

Choose 3M and get the throughput you need in the process.

Selecting the processor for your needs is not always easy.

You've got to take into account available space, amount of usage, and the future capacity of your department, including emergency back-up.

That's why 3M give you two choices in processors—the XP 507 and the XP 510 C. Separately or in combination, they give you the throughput and flexibility you need. Ask your 3M representative for more details, or contact Alan Budge,
3M House, P.O. Box 1,
Bracknell, Berkshire,
RG12 1JU.
Tel. Bracknell 58458.

3M and Trimax are trade marks.

3M

Fischer Ultrasound Ltd.
The Royal Free School of Radiography

Diagnostic Ultrasound Training Courses

March 2nd – 6th, 1981

Introductory Course for Radiographers/Clinicians/Physicists/Radiologists with little or no previous experience of Diagnostic Ultrasound.

March 9th – 13th, 1981

Current Trends in Diagnostic Ultrasound for Radiographers/Clinicians/Physicists/Radiologists with experience in Ultrasound.

For application forms and further details please contact:-

Fischer Ultrasound Courses,
c/o Mr. Bill Smith,
Superintendent Radiographer,
The Hoo,
17 Lyndhurst Gardens,
London, N.W.3.

RADIOLOGIST

Large group diagnostic radiological practice with multiple departments; private nursing homes and hospital appointments requires assistants and or partners.

Facilities for specialised diagnostic disciplines.

Group based in Johannesburg, South Africa.

Please write to:

The Senior Partner,
P.O. Box 4878,
Johannesburg.
2000
Republic of South Africa.

THE ROYAL COLLEGE OF RADIOLOGISTS

First Examination for the Fellowship

HONG KONG—SEPTEMBER 1981

The First Examination for the Fellowship of the Royal College of Radiologists in Radiodiagnosis and in Radiotherapy and Oncology will be held in Hong Kong in September, 1981. To be eligible to take this examination candidates must have completed the necessary training in departments recognized by the Royal College of Radiologists.

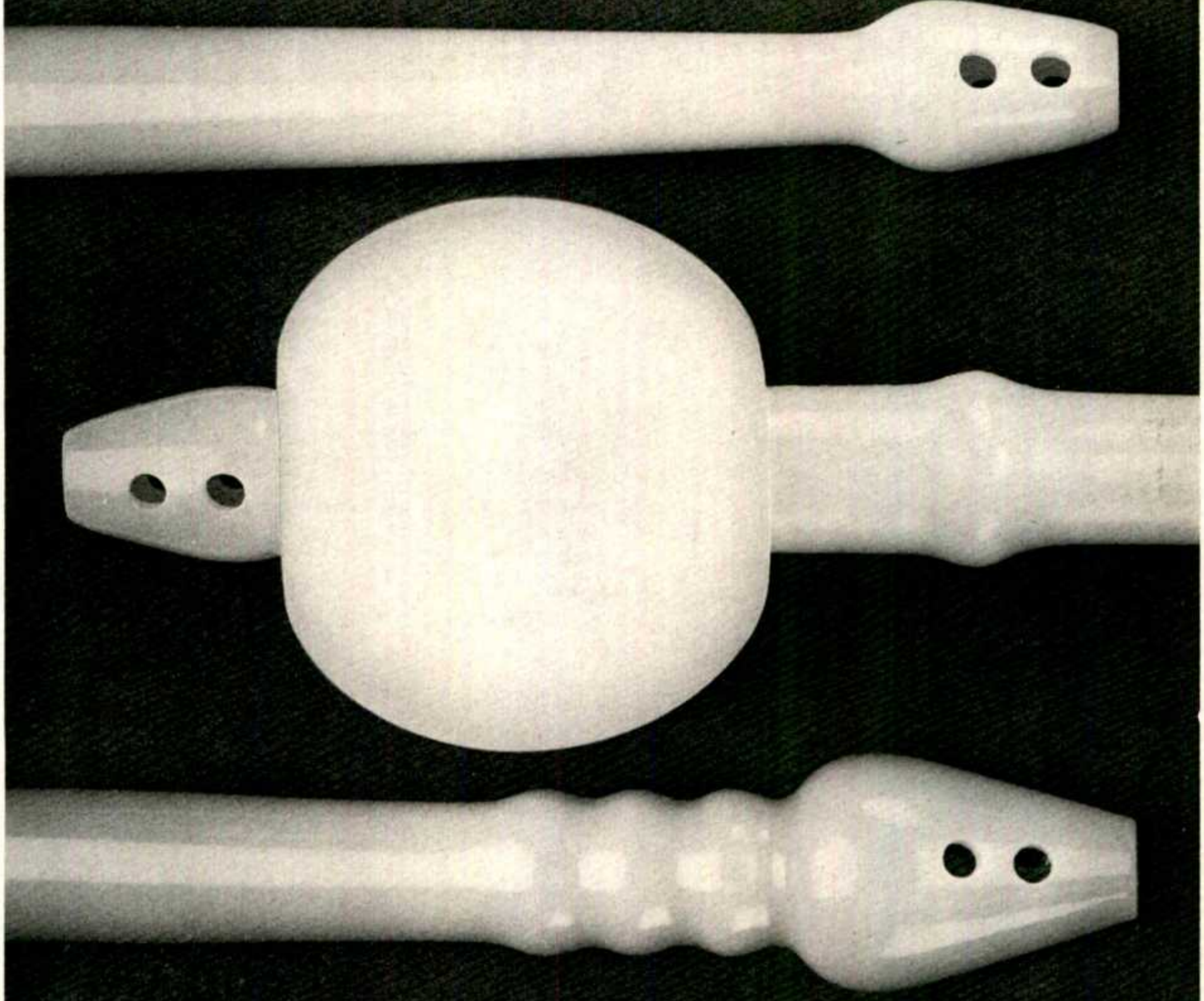
The written papers will be held on 7th and 8th September, 1981, and the oral examinations will commence shortly afterwards. The closing date for applications is the 15th May, 1981, and applications received after this date cannot be accepted.

Further information and application forms may be obtained from the

Examinations Secretary, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG.

When requesting an application form, applicants are asked to indicate clearly that it is the examination in Hong Kong which they wish to take.

Take a tip from us...



E-Z-EM®

A complete range of super-smooth flexible PVC tips available.
* Double contrast tips
* Balloon tips for elderly patients
* Paediatric tips for newborn and young children

Full details from:

Henleys Medical Supplies Ltd. London N8 0DL Tel: 01-889 3151

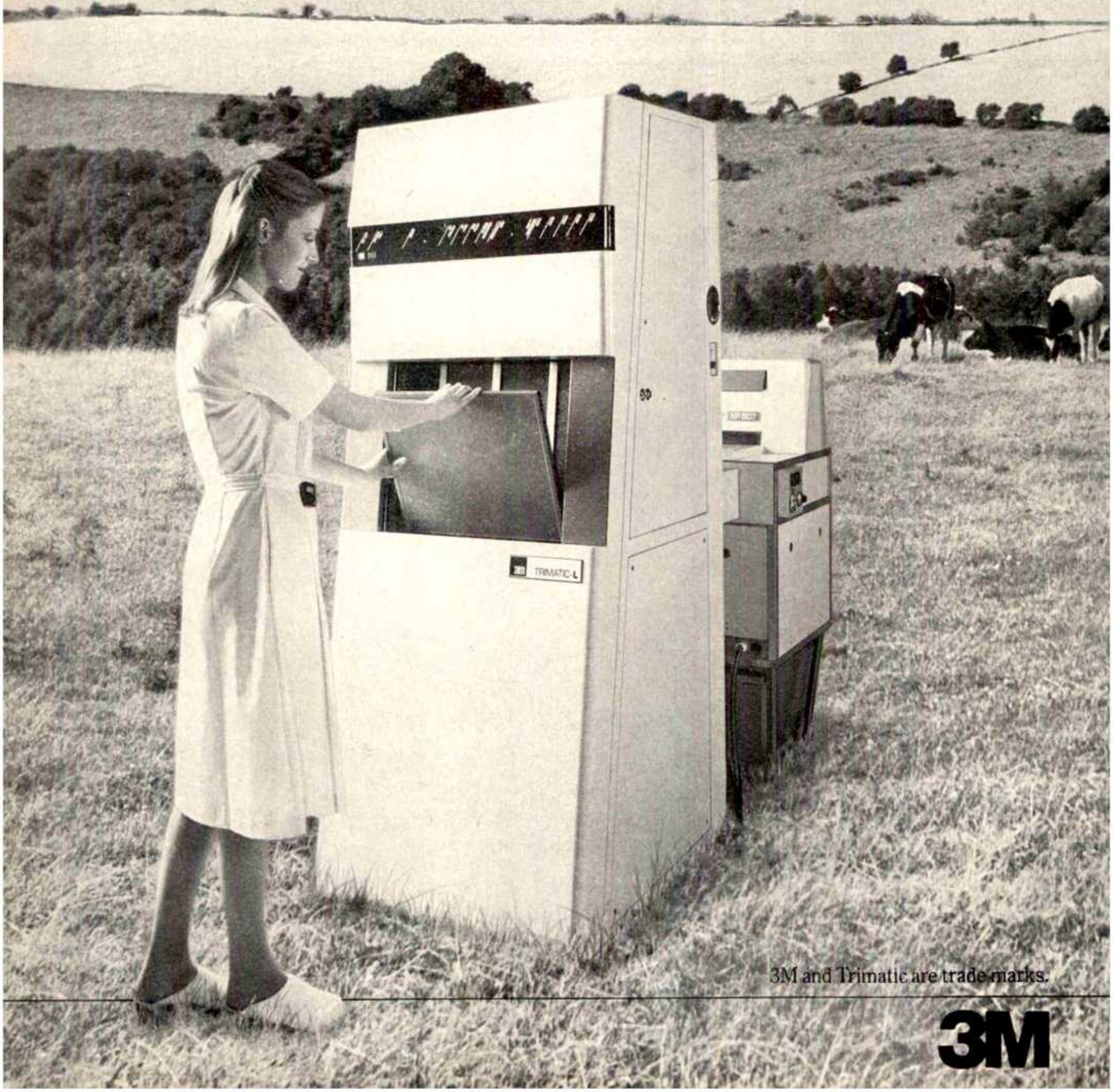
Produced by E-Z-EM Ltd. London.

Now there's a fully integrated, fully automatic film handling and processing system that makes daylight radiography a total daylight process. From loading the film magazine right through to producing the finished radiograph, the Trimatic Daylight Loading System from 3M brings daylight radiography truly out of the shade.

But it has to be experienced to be believed.

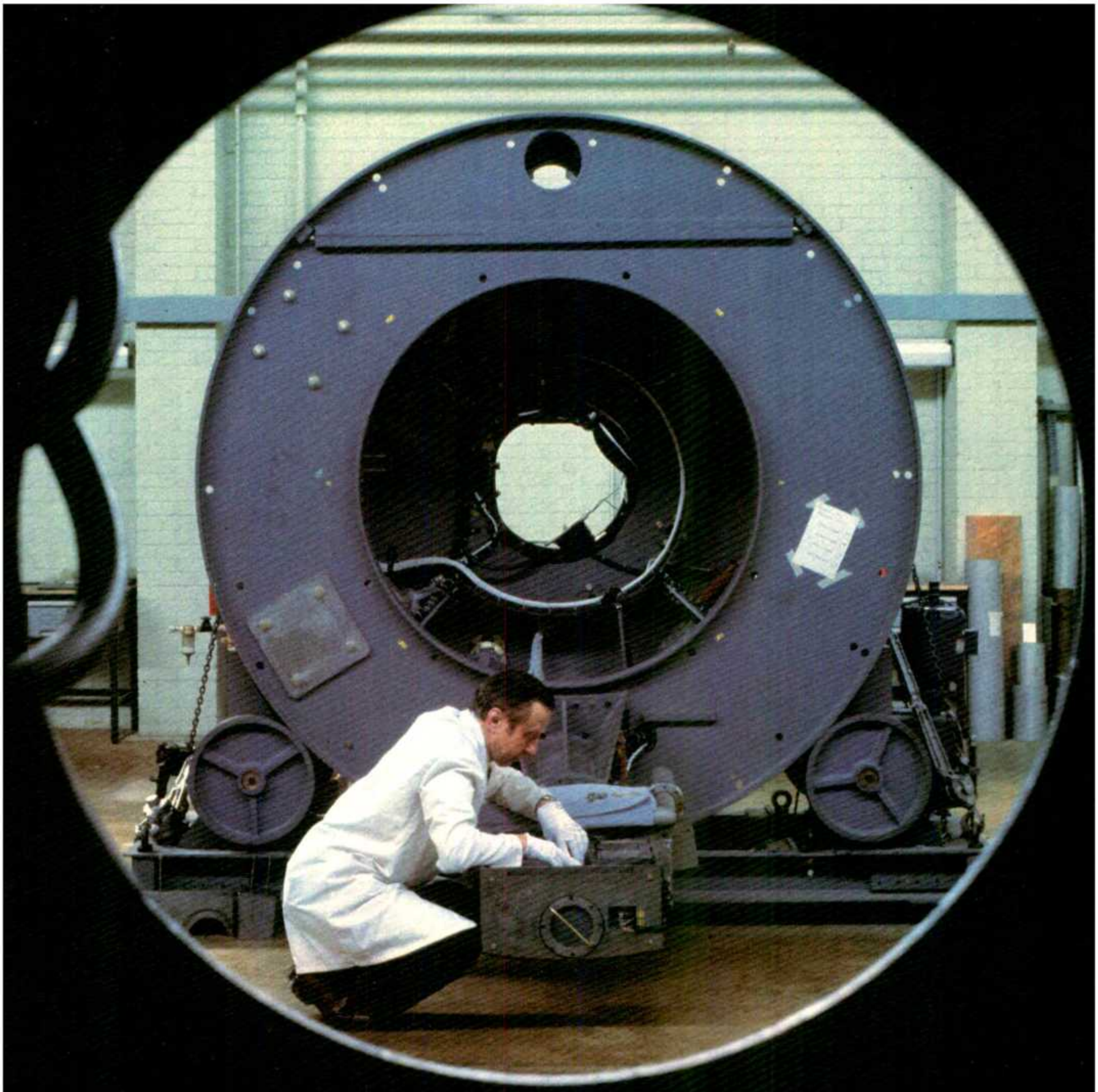
For detailed information just ring Alan Budge on Bracknell (0344) 58458 or write to him at X-Ray Products,
3M United Kingdom Ltd, FREEPOST, Bracknell, Berkshire RG12 1BR.

THE TRIMATIC DAYLIGHT SYSTEM:
IT DOES WHAT OTHER
DAYLIGHT SYSTEMS CAN'T.



3M and Trimatic are trade marks.

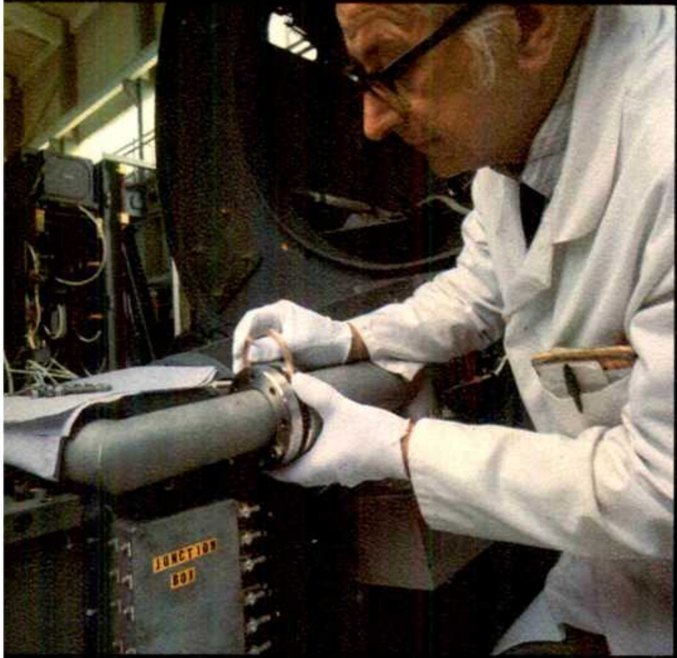
3M

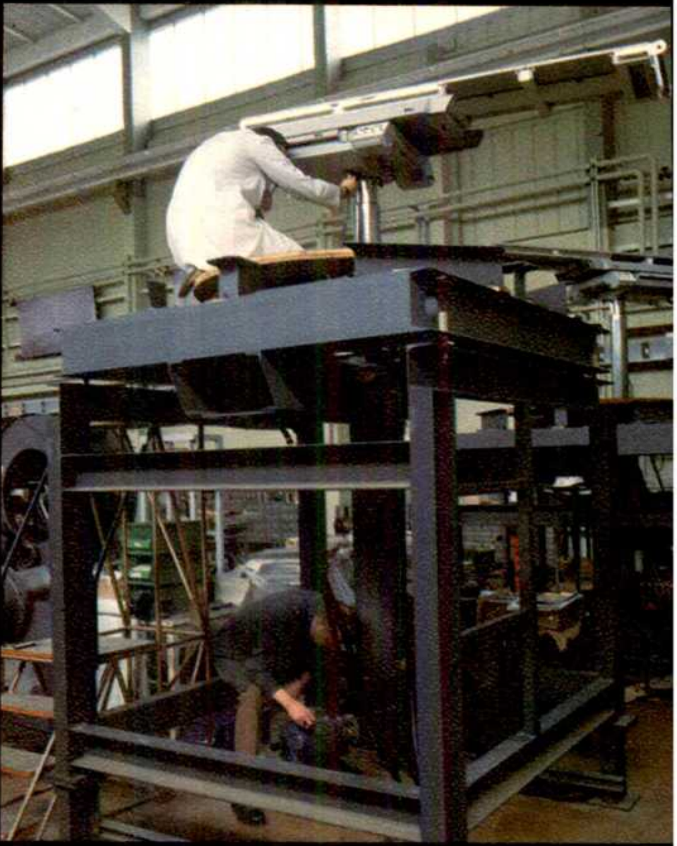


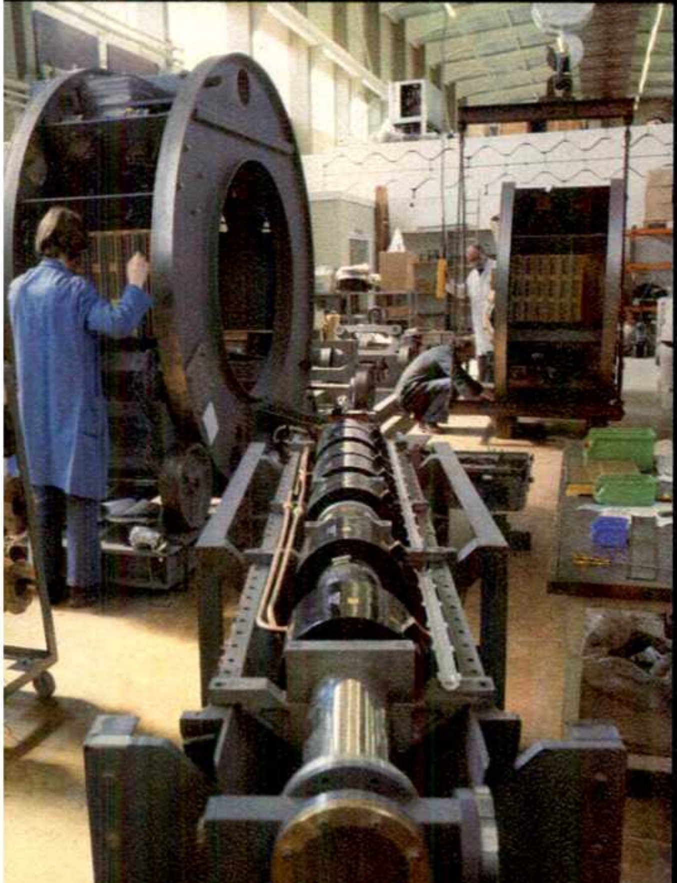
From their inception Philips linear accelerators have been designed to meet the most exacting requirements in radiation therapy. Today they represent a unique product of 1980's technology and craftsman engineering.

As new clinical demands materialise, Philips ongoing commitment guarantees their realisation.

Meticulous attention to detail-
The Philips hallmark.



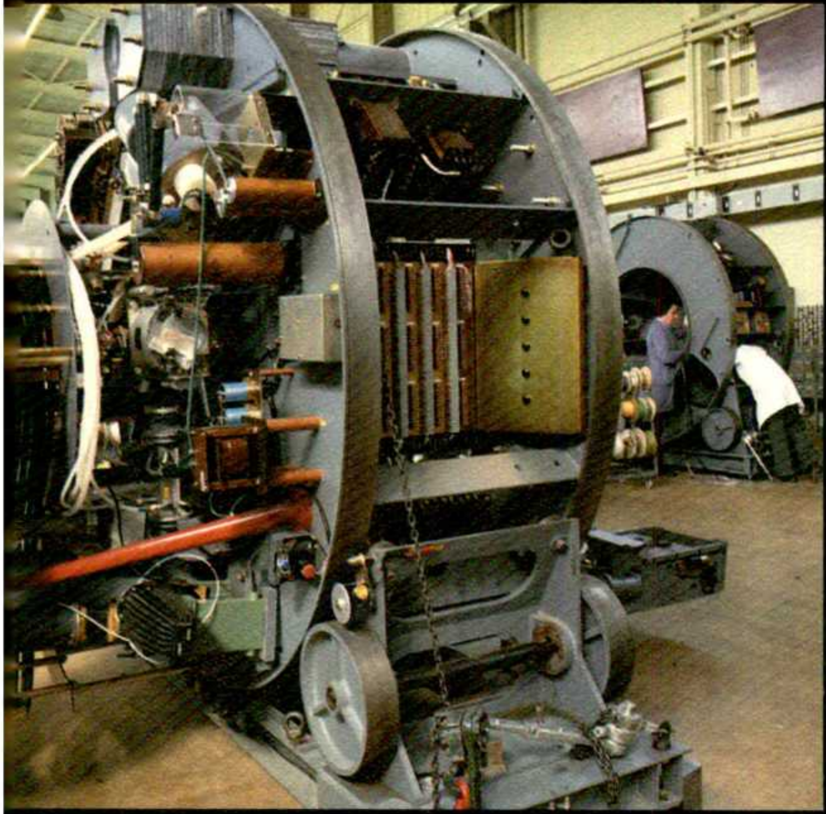




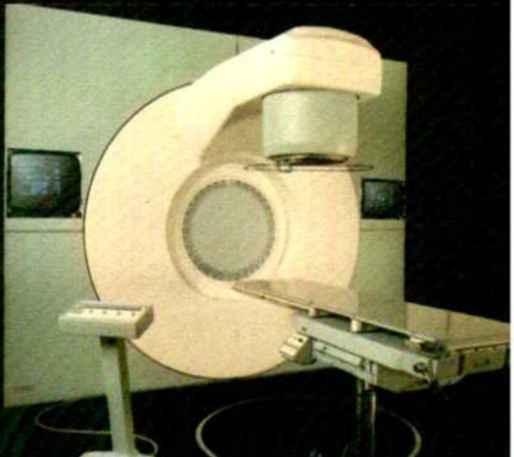
In design Philips linear accelerators are in the forefront of modern technology. In production they are in the hands of skilled, specialist craftsmen.

PHILIPS

30 years specialised experience-
The foundation for the future.



The new microprocessor
treatment control console.



Stringent performance testing for the clinical demands ahead.

Medic

art of the Philips medical linear accelerator factory, Crawley, England.

Contact Philips at one of the addresses shown below
for more information on our full range of equipment for radiation therapy.

Philips Medical Systems, Kelvin House, 63/67 Glenthorne Road, Hammersmith, London W6 0LJ.
M.E.L. Manor Royal, Crawley, Sussex RH10 2PZ.
Divisions of Philips Electronic & Associated Industries Ltd.
Philips Medical Systems Inc, 710 Bridgeport Avenue, Shelton, Connecticut 06484, United States of America.
N.V. Philips, Medical Systems Division, Eindho[illegible], The Netherlands.

new books from Blackwell

X-ray Diagnosis

Peter Armstrong M.B. B.S. F.R.C.R. and Martin L. Wastie M.B. B.Chir. M.R.C.P. F.R.C.R. Early 1981. 360 pages, 564 illustrations. About £15.00

This title is designed as a textbook of diagnostic radiology for the medical student and newly qualified doctor. For each body system a number of basic signs are described and the differential diagnostic possibilities explored. The book aims to teach students how to look at X-ray films as well as the radiological signs in different diseases. Short accounts of ultrasound examinations are included to show their place in diagnosis.

Nuclear Medicine: an Introductory Text

P.J. Ell M.D. M.Sc. and E.S. Williams M.D. Ph.D. F.R.C.P. March 1981. 288 pages, 211 illustrations. About £16.50

With the increasing use of 'high technology' as a diagnostic and clinical aid to medical and surgical techniques, it is more necessary than ever to have a reliable, modern and introductory text to this subject. This book is a good lead towards specialist monographs and does not seek to replace them. It does, however, fill the clinical gap and informs radiologists, oncologists and clinicians of the wide range of nuclear medicine facilities and explains to medical scientists and technicians involved with radioactive materials the clinical relevance of their work.

Uroradiology

Thomas Sherwood M.A. M.B. D.C.H. F.R.C.P. F.R.C.R. 1980. 360 pages, 435 illustrations. £35.00

'It will become the standard textbook of radiological findings in urological disease, and it is recommended without hesitation for all surgeons and radiologists who deal with diseases of the genito-urinary system.' *British Journal of Surgery*

Essential Physics for Radiographers

J.L. Ball T.D.C.R. and A.D. Moore T.D.C.R. 1980. 272 pages, 203 illustrations. Paper, £6.50

Gynaecological Radiology

G.H. Whitehouse M.B. B.S. M.R.C.P. F.R.C.R. March 1981. 248 pages, 257 illustrations. About £22.50

As well as covering the more specific investigations which pertain to the genital tract, it is shown that other standard radiodiagnostic procedures and the recently introduced modalities of ultrasonography and computerised axial tomography, are applicable to the gynaecological patient. This monograph will prove highly useful to postgraduates in diagnostic radiology and gynaecology, both in training and as consultants.

Lecture Notes on Clinical Oncology

B.W. Hancock M.D. M.R.C.P. D.C.H. and J.D. Bradshaw M.B. Ch.B. F.R.C.R. D.M.R.T. Early 1981. 208 pages, 12 illustrations. Paper, about £5.00

These *Lecture Notes* present an up-to-date guide to the theory and practice of all aspects of clinical oncology and provides insight into the diverse nature of the subject. The multidisciplinary approach, which is so necessary for the successful management of any cancer patient, is strongly emphasized. All senior undergraduate students and recently qualified practitioners in any speciality will find this new title invaluable.

Clinical Radiology in Gastroenterology

C.I. Bartram M.B. M.R.C.P. F.R.C.R. and Parveen Kumar M.D. M.R.C.P. Summer 1981. 216 pages, 425 illustrations. About £20.00

This book analyses the role of radiology, including ultrasound and CT scanning, in disorders of the gastrointestinal tract, liver and pancreas. The radiological findings are discussed and illustrated with many clear line diagrams and the emphasis throughout expresses the value of radiological investigation of gastrointestinal problems.

Real-time Ultrasound in Obstetrics

Edited by M.J. Bennett M.D. M.R.C.O.G. F.C.O.G. and S. Campbell M.B. B.S. F.R.C.O.G. 1980. 160 pages, 88 illustrations. £15.00

Blackwell Scientific Publications

Nuclear Medicine Communications

*International
*Rapid publication
*Newsletter section

Editors

K E Britton, MD, MSc, FRCP, St Bartholomew's Hospital, London
P J Ell, MD, MSc, The Middlesex Hospital Medical School, London
R F Jewkes, MB, BS, FRCP, Charing Cross Hospital, London

The Nuclear Medicine community has until recently lacked a vehicle for the rapid communication of new research. *Nuclear Medicine Communications,* which commenced publication in 1980, now provides this service. In general, authors' papers are published not more than three months after acceptance.

Created on the initiative of the British Nuclear Medicine Society, and guided by an international board of advisory editors, the new journal is an English language forum for short original papers of high quality. In addition, it provides a newsletter section, in which reports of major conferences and other significant events are included.

Contributors: Full details for submission of articles are given on the inside back cover of the journal, or on application to one of the editors.

Subscribers: Sample copies are available from the publishers. Six issues published per year, totalling approximately 384 pages.
Rates: UK, £24.00 p.a.; overseas £27.50 p.a.

CHAPMAN AND HALL
The Scientific, Technical and Medical Division of
Associated Book Publishers Ltd.,
11 New Fetter Lane, London EC4P 4EE

HEINEMANN

A Practical Introduction to Cranial CT

A. R. Valentine, P. Pullicino and E. Bannan

This book is designed to introduce doctors and technical personnel to the application of CT in neurological and neurosurgical diagnosis. It should become essential reading as CT becomes even more widely available and accepted. It will be particularly relevant to radiologists, and also to neurological clinicians, both medical and surgical and most useful for those encountering the technique for the first time. But established practitioners will also benefit much from an up-to-date synopsis as well as reiteration of some technical and anatomical details.

The text is extensively illustrated throughout.
ISBN 0-433-33602-1 160 pp £8·00

Also available:

C. Metreweli: Practical Abdominal Ultrasound

This book fulfils a need for anyone learning how to use diagnostic ultrasound in obstetrics and in general abdominal investigation.
ISBN 0-433-21311-6 160 pp £15·50

Coming in February:

Clark's Positioning in Radiography

Vol. 2 The extensively revised 10th Edition by Louis Kreel.
ISBN 0-433-188332 448 pp £22·50

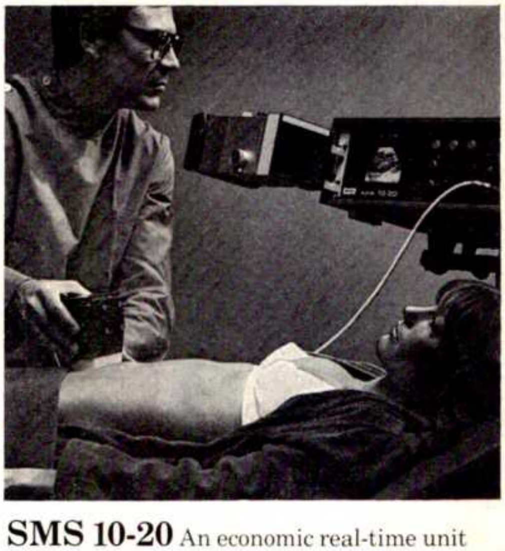
William Heinemann Medical Books Ltd
23 Bedford Square, London WC1B 3HH

Ultrasound

TOMORROW'S TECHNIQUE FOR TODAY'S DIAGNOSES

Varian V3000 the ultimate in phased array ultrasonography, with a wide choice of image storing sub-systems.

Generex general purpose scanner for abdominal studies, obstetrics and cardiology.



SMS 10-20 An economic real-time unit with an easily manipulated transducer head.

CGR

Full details and specifications from
CGR MEDICAL LIMITED
Astronaut House, Feltham, Middx. Tel: 01-890 8166
Branches at: *Iristol, Cambridge, Edinburgh, Glasgow, Manchester, Nottingham.*

MOBALTRON
MS
80

The Mobaltron M S 80 is one of the most sophisticated cobalt 60 units in the world, complying fully with R.A.S.M.P. 75 and having the following features:

- 40 x 40 cm field size at 80 cm.
- 10,000 RHM head capacity.
- Full interlock and confirmation circuits.
- Digital readouts.
- Dual timer.
- Variable speed motorised movements.
- Split spine treatment table.

The Mobaltron M S 80 can also be supplied as a computer controlled tracking unit.

TEM

TEM Instruments Limited
Gatwick Road, Crawley, Sussex. RH10 2RG, England
Tel: 0293 31244 Telex: 87397 Grams: TESTMENT CRAWLEY

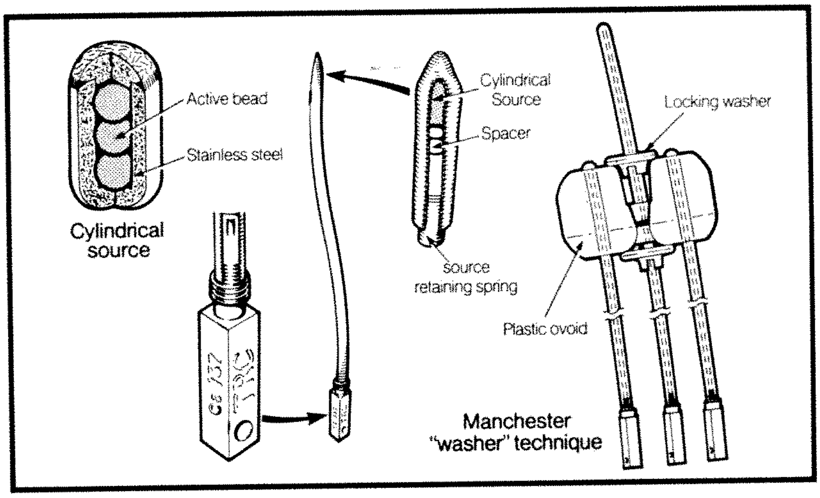
Our Afterloading Systems put brachytherapy right on target

With the addition of our new caesium-137 gynaecological afterloading system, we now supply a comprehensive range of products for intracavitary and interstitial radiotherapy.

Intracavitary radiotherapy

Our caesium-137 "Manchester" afterloading system consists of X-Ray opaque PVC applicators which allow the "washer," "spacer" or "tandem" techniques to be used. The guide tubes are flexible and have a diameter of only 6.3 mm overall. Complete kits are supplied sterilized in packaging designed for maximum convenience in use.

The sources contain glass beads in welded stainless steel capsules assembled into flexible source trains for which special shielded containers are supplied. Iso-dose curves are available for each source train. Individual sources and source trains are also supplied for most of the currently available remote afterloading systems.



Interstitial radiotherapy

Our iridium-192 flexible wire afterloading systems include complete sets of applicators and accessories for the Pierquin/Paine technique. All accessories for these systems are pre-packed ready for use and sterilized where necessary. Platinum clad iridium-192 wire in 500 mm lengths is readily available in activities up to approximately 0.3 mCi/mm providing exposure rates of up to 0.16 mR per hour at 1 metre.

Iridium-192 "hairpins" and single pins: Thicker platinum coated iridium-192 wire is supplied pre-shaped as "hairpins" and single pins for use with slotted guide needles which are made in stainless steel to the designs of Pierquin and Paine.

The Radiochemical Centre
Amersham

Full information is available on request.
The Radiochemical Centre Limited, Amersham, England. Telephone: 024-04-4444
In the Americas: Amersham Corporation, Illinois 60005. Telephone: 312-593-6300
In W. Germany: Amersham Buchler GmbH & Co KG, Braunschweig. Telephone: 05307-4691
1885

FARMER
DOSEMETER
2570

A New Generation Microprocessor System

Improved accuracy, precision and simplicity of operation are major features in this new generation microprocessor dosemeter. Facilities include: a fully auto-corrected readout with keyboard entry of pressure, temperature and chamber correction factors; and keyboard entry of time for measurement of dose and exposure rate.

Operator's error is minimised by arrangement of controls, and the information display indicates mode of operation, corrections applied, and unit of measurement.

The fully portable and battery operated 2570 is offered with a 0.6cm^3 chamber which is conveniently housed in the instrument case. Calibrated in exposure (roentgens) internal links permit scaling in grays (absorbed dose).

Full details on request.

SAFETY FEATURES

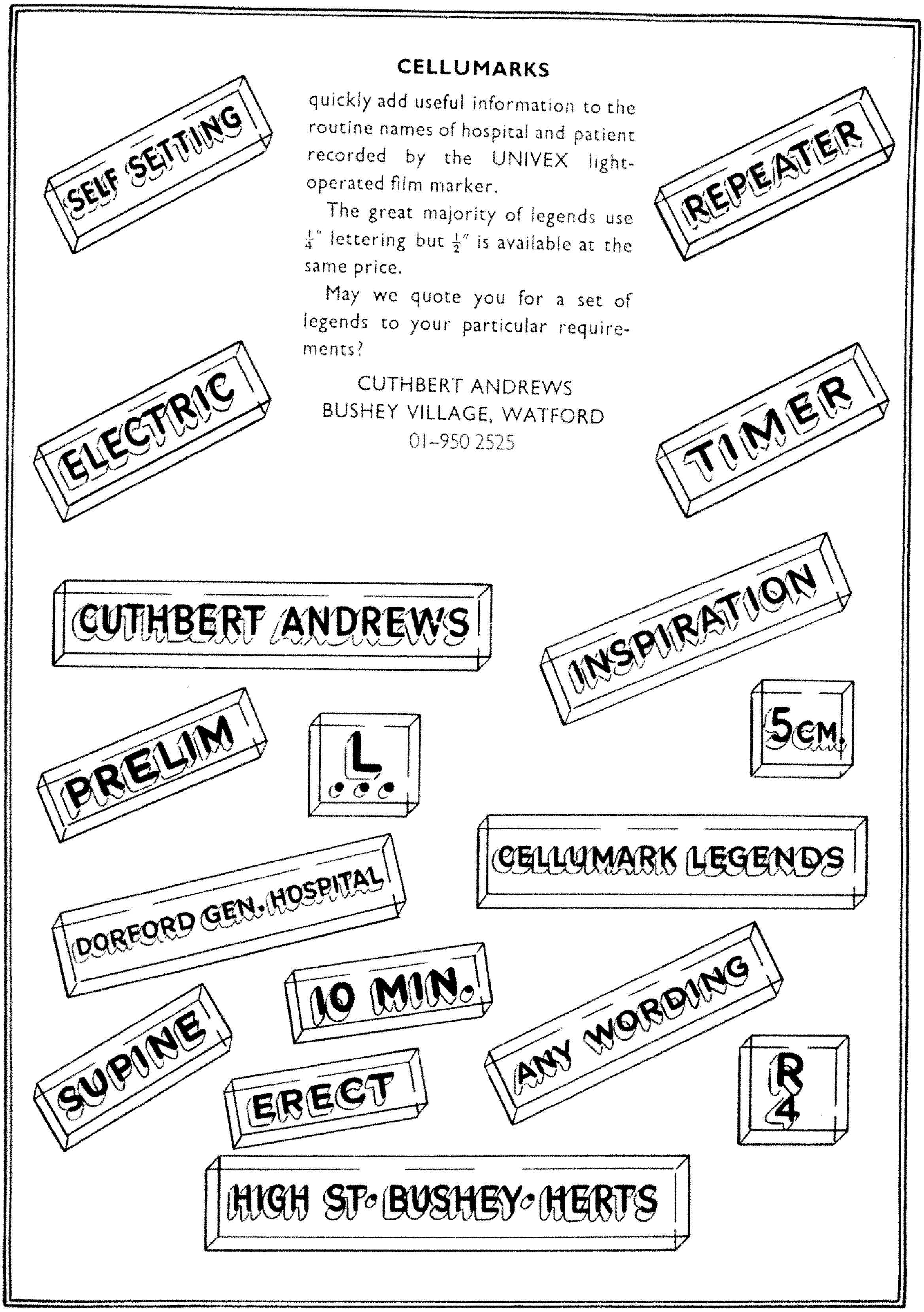
- Keyboard disabled during measurement.
- Measurement aborted if switches are operated during measurement.
- Built-in display clock.
- Indication of "off zero" condition and adjustment required clearly shown on information Display.
- Measurement of applied dose, if any, continues even after Trip Output is actuated.
- Elimination of range setting errors.
- Unit of measurement and associated prefix displayed automatically.

NUCLEAR ENTERPRISES LIMITED

1979

Bath Road, Beenham, Reading, RG7 5PR, England.
Tel: 073-521 2121. Telex: 848475.
Cable: Devisotope, Reading.
Also at: N.E. Nuclear Enterprises, Geneva.
Nuclear Enterprises GmbH, Munich.
Nuclear Enterprises, San Carlos, U.S.A.

UNIVERSITY COLLEGE OF MEDICINE
LIBRARY



CELLUMARKS

quickly add useful information to the routine names of hospital and patient recorded by the UNIVEX light-operated film marker.

The great majority of legends use ¼" lettering but ½" is available at the same price.

May we quote you for a set of legends to your particular requirements?

CUTHBERT ANDREWS
BUSHEY VILLAGE, WATFORD
01–950 2525

1981, *British Journal of Radiology*, *54*, 91–102

VOLUME 54 NUMBER 638 FEBRUARY 1981

The British Journal of Radiology

Positron-emitting radionuclides in the study of metabolic and physiopathologic mechanisms

Mackenzie Davidson Memorial Lecture, April 1980

By C. Kellershohn

Service Hospitalier Frédéric Joliot, Département de Biologie, Commissariat à l'Energie Atomique, Hôpital d'Orsay, 9100 Orsay, France

To be invited to give the Mackenzie Davidson Memorial Lecture is for me a great honour, although a formidable one. Formidable because I doubt that the modest level of my scientific contribution is worthy of honouring the memory of a man of the stature of Sir James Mackenzie Davidson, and because I have been preceded in this task by so many men of science and medicine who are among the most eminent of our era since the first lecture given in 1920 by Lord Rutherford.

Nevertheless, the memory of my first publications which dealt with "after-image effects" and the phenomenon of colour adaptation, and the fact that my own evolution began with physiological optics and evolved into the techniques of nuclear imaging and the application of nuclear physics to the study of biological processes and structures, give me some courage to address you. For Sir James Mackenzie Davidson, who was born in Argentina in 1856, practised as an ophthalmologist in Aberdeen after completing his medical studies in that city. Within the space of one year, Röntgen in 1895 and Bécquerel in 1896 discovered X rays and radioactivity, which have profoundly influenced the evolution of physics and furnished medicine with powerful tools, influencing even the processes of diagnosis and therapy. This crucial year provided Sir James with the opportunity to begin his work with the creative imagination, intuition, versatility and curiosity which characterized his personality. Immediately recognizing the importance of a discovery apparently outside his discipline, this ophthalmologist made a trip to Würzburg in 1896 in order to assimilate all the information which he could obtain from Röntgen. In 1897, he left Aberdeen to settle in London where he was elected to the staff of the Charing Cross Hospital as an ophthalmologist and where he participated with Professor Sylvanus Thompson in founding the Roentgen Ray Society which today is The British Institute of Radiology. In that year Mackenzie Davidson and Hedley (1897) published a paper describing a method for the precise localization, to within a hundredth of an inch, of foreign bodies in an organism by means of X rays. Taking advantage of his knowledge of optics, he established the basis of stereoradiography at the same time. From then on, Sir James's remarkable evolution led him from ophthalmology to the medical applications of X rays, in terms of both diagnosis and radiobiology (Mackenzie Davidson, 1912). This capacity for recognizing the importance of a new field, which was so different from his original orientation, was (and still is) the characteristic of a great scientific mind and made him the leader of British radiology until his death in 1919.

It seems likely to me that if Sir James had been in his forties in 1934, another crucial year, that of the discovery of artificial radioactivity by Irène and Frédéric Joliot, his intuition would have led him to evolve from ophthalmology to the use of nuclear indicators in studying physiological processes and their pathological modifications. As the evolution of Sir James indicates so strikingly, the medical implications of Röntgen's discovery were immediately recognized by the medical profession and quickly led to the birth of a new discipline, radiology. The same was true for artificial radioactivity, as shown by the fact that Frédéric Joliot was elected a member of the French Academy of Medicine soon after discovering it. This discovery, involving radioisotopes of each element in the periodic table, led to the possibility, at first sight, of a multitude of applications in the fields of therapeutics and clinical investigation.

Metabolic Investigation and Nuclear Medicine

I will not discuss the therapeutic applications of artificial radionuclides which are rather limited and which do not enter the scope of my address. In terms of functional investigation, the use of radioisotopes has spread extensively and has led to the development of a new medical field known as nuclear medicine, a term which may be questioned but is today almost universally used. The possibility of quantitatively following—due to its radioactivity—the metabolic kinetics of a labelled element or molecule associated with the function of an organ allowed researchers to determine the functional state of the organ along with the consequence which this implies from a diagnostic and prognostic point of view. The existence of γ-emitting nuclear indicators made the method especially attractive in medicine by allowing non-invasive measurements by external detection of such radiation, without taking any sample from the organ involved. In 1940, Hamilton and Soley, using γ-emitting ^{128}I and a Geiger counter placed over the isthmus of the thyroid, were able to differentiate between the iodine metabolism of normal and hyper- or hypo-thyroid patients.

This is not the place to develop the many applications of the method, which is part of the nuclear medicine arsenal, such as the investigation of the permeability of the biliary tract using labelled dye, the study of ventilatory and circulatory functions of the lung using rare gases and labelled microspheres, the investigation of renal function using labelled hippuran, or the many haemodynamic methods of investigation using nuclear indicators of blood kinetics.

Following the development of scanning methods in the early 1950s (Cassen *et al.*, 1951; Mayneord and Newbery, 1952), and of the gamma camera by Anger (1958), the anatomical aspects of nuclear imagery associated with the detection and localization of lesions are still stressed in nuclear medicine. The indicators used to visualize lesions such as cysts, abscesses, malignant tumours and inflammatory lesions have been salts or complexes of various metals, particularly ^{99}Tc^{m} and to a lesser extent ^{113}In^{m}, ^{67}Ga, ^{57}Co, ^{203}Hg and ^{197}Hg. This orientation has been in large part due to the incapacity of conventional radiodiagnostic methods to visualize soft tissues except in a few cases. Faced with this situation, nuclear imaging has been of real interest despite its poor quality. This has now considerably changed following the introduction of X-ray transverse axial tomography by Hounsfield (1973) after the pioneering work of Cormack (1963; 1964) and the remarkable development in the last few years of ultrasonic imaging techniques as indicated, among others, by Ian Donald (1976) who delivered the Mackenzie Davidson Memorial Lecture five years ago. The appearance of these techniques, which provide images of soft tissue with incomparable sharpness, has almost made obsolete the use of nuclear images for anatomical purposes. In my opinion this situation has produced a kind of crisis from which nuclear medicine has not completely recovered.

If we consider the different functional investigation techniques of nuclear medicine, we realize that they cover certain aspects of physiology but not at all what has been referred to properly as metabolism. Many biological phenomena such as the passage of a molecule through a membrane, the enzymatic degradation and the selective uptake of a substance by a receptor site, all of which can be used for important medical applications, have not been taken into consideration by nuclear medicine until recently. This is quite illogical, as from the very beginning of the discovery of artificial radioactivity, and after the work of Von Hevesy (1948), this aspect of the use of nuclear indicators seemed of major interest to all. Since then much work on animals using such indicators as ^{14}C, ^{3}H, ^{32}P and ^{35}S has considerably expanded our knowledge of metabolic processes and their defects. The above-mentioned radioelements have been used because, along with oxygen and nitrogen, they correspond to the essential constituents of most molecules taking part in these processes. But these radioelements are all pure β-emitters which cannot be detected in an organ by non-invasive methods; this practically excludes their use in man. This explains why the study of metabolic processes for purposes of functional investigation in man has been so infrequently taken up by nuclear medicine.

Place of the Three Nuclides ^{15}O, ^{13}N, ^{11}C

If we consider the approximately 1500 artificial radioelements known today, the number which are isotopes of the major constituents of molecules involved in metabolism and which are detectable from outside the organism and have a half-life which makes them usable is limited to three: ^{15}O with a half-life of two minutes, ^{13}N with a half-life of ten minutes and ^{11}C with a half-life of 20 minutes. These three elements are pure positron emitters which can be detected from outside the organism by γ rays arising from the annihilation of these particles. They can only be obtained by nuclear reactions with charged particles, and in practice this means by the use of a cyclotron. Because of their short half-lives they must be produced at the site of utilization. This requires, therefore, a cyclotron in the hospital environment. The importance of the location of such a machine in a hospital was first perceived in this country, where the cyclotron installed by the Medical Research Council at Hammersmith Hospital has been operating now for 25 years (Newbery, 1959). Progress since that time in the development of small isosynchronous compact cyclotrons for medical use, as well as the growing interest in neutron therapy and in the possibility of carrying out functional investigations with short-lived positron emitters, has resulted in multiplication of the British experiment, notably in the United States. Similarly, we have had at our disposal for eight years at the Service Hospitalier Frédéric Joliot of the Department of Biology of the Atomic Energy Commission of France a cyclotron which is utilized in large part for the production of these three radioelements. Today some manufacturers are proposing, for the production of these three radionuclides, small self-shielded push-button cyclotrons, which can be operated with confidence by non-specialized personnel. Apart from financial considerations, it is not these machines which are likely to limit the use of ^{15}O, ^{13}N and ^{11}C in medicine. One important limiting factor has been the poor performance of conventional gamma cameras for the 511 keV photons from the positron emitters. In effect, study of the kinetics of a labelled molecule requires measurement of the variation in the concentration of radioactivity in the zone of interest obtained from a sequence of corrected tomographic images. This limitation has been partly alleviated in recent years by the development of various positron tomographic cameras (Phelps *et al.*, 1975; Brownell and Burnham, 1973; Yamamoto *et al.*, 1977; Ter-Pogossian *et al.*, 1978).

Today the positron emission tomograph developed by Phelps is being produced commercially by ORTEC in the form of the ECAT (Emission Computerized Axial Tomography). Many problems must still be solved before these cameras can make absolutely accurate quantitative measurements. Nevertheless, they represent great progress and allow a sufficient estimate of the relative concentrations of radioactivity.

Of the three radioelements considered, ^{15}O is the simplest to use. The extremely short half-life of two minutes in effect excludes, except in a very special case which we will consider, its utilization for labelling molecules. Its field of application is thus limited, but at the same time one avoids the complex problems encountered in the synthesis of labelled molecules.

USE OF OXYGEN 15

It is 20 years now since the utilization of ^{15}O was proposed by Ter-Pogossian and Powers (1958) to

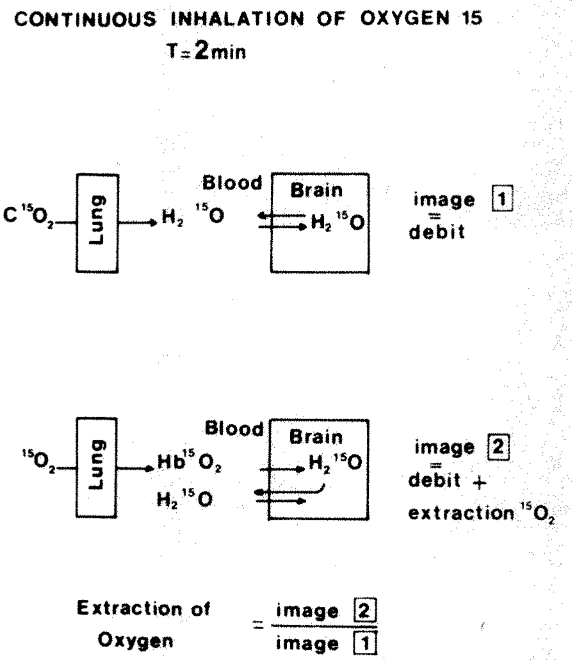


FIG. 1.

Model for the determination of blood flow and coefficient of extraction of oxygen by cerebral tissue using continuous inhalation of $C^{15}O_2$ and $^{15}O_2$.

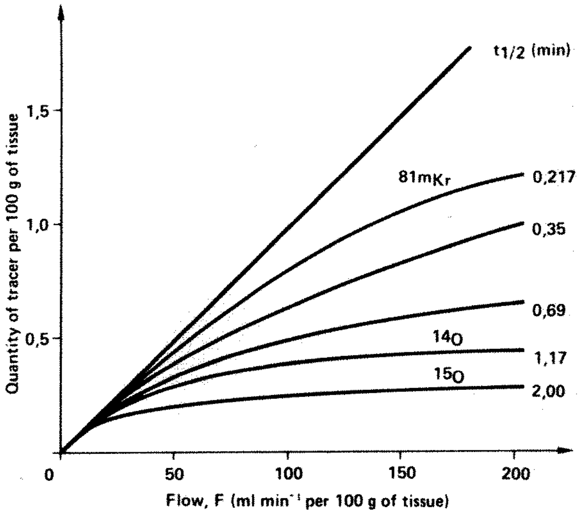
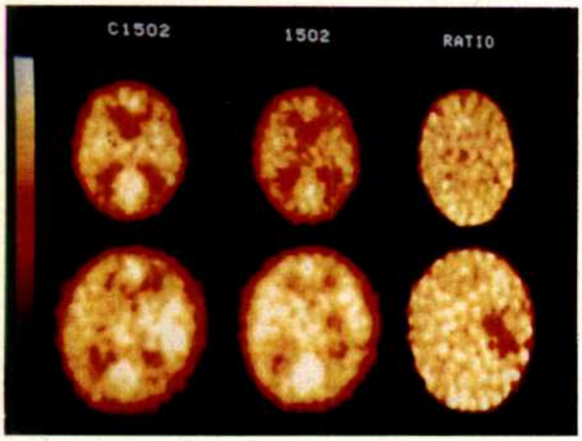
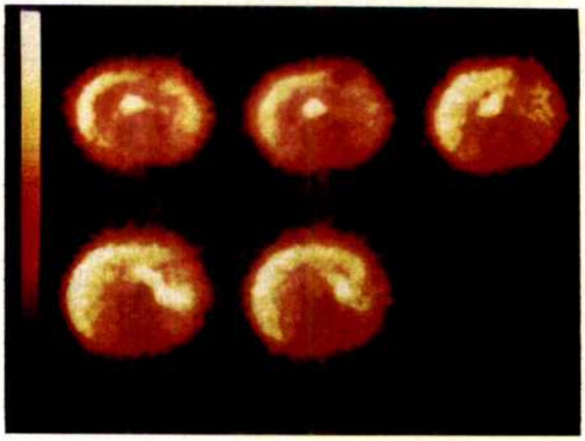
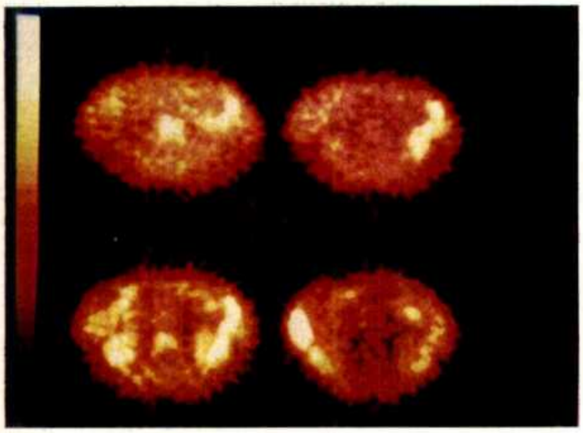


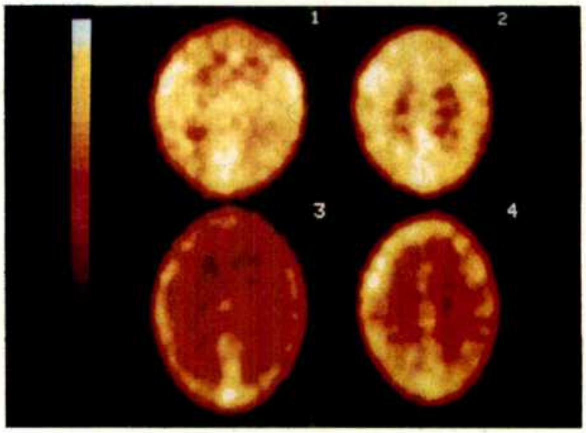
FIG. 2.

The relation between blood flow and cerebral tissue radioactivity in the stationary state, for tracers of different half-lives.


C1502
1502
RATIO






1
2
3
4

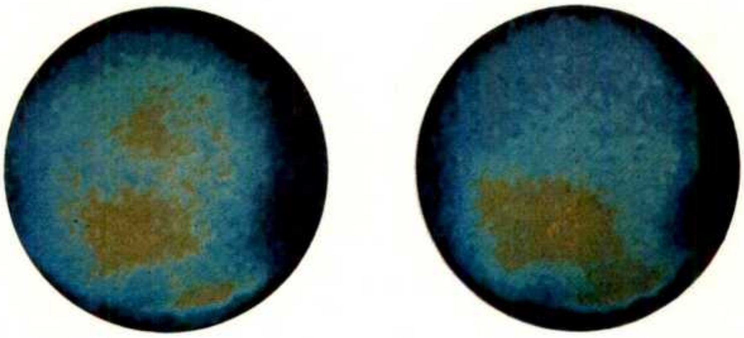


FIG. 3 (*facing page, top left*).

Distribution of oxygen extraction for cerebral tissue. From left to right: image of a brain slice after continuous inhalation of $C^{15}O_2$, then after inhalation of $^{15}O_2$, and finally the distribution of the ratio of the two images: above, normal subject; below, subject suffering from a recent infarct. One can see in the first image the hyperperfusion of blood at the level of the infarct, which is well defined in the third image.

FIG. 8 (*facing page, top right*).

Abdominal tomographic slices at five successive adjacent levels above the umbilicus in a normal subject after injection of ^{11}C-methionine. From left to right and from top to bottom there appear successively the head, body and tail of the pancreas.

FIG. 9 (*facing page, centre left*).

Transverse tomographic images of the pancreas with ^{11}C-methionine in a subject presenting with cancer of the head of this organ. One can see in the intermediate slice, above and to the right of the figure, the disappearance of the image of the pancreas. This indicates that the tumour, which does not fix methionine, should be found at this level.

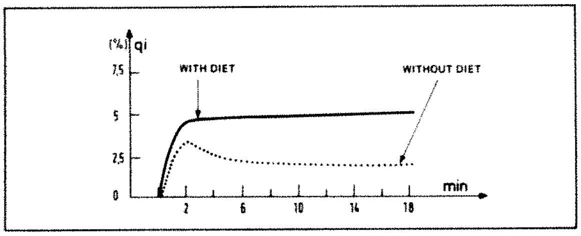


FIG. 10 (*and facing page, bottom*)

Cerebral fixation of methionine in a phenylketonuric child on a diet lacking phenylalanine (left) and on a normal diet (right).

FIG. 11 (*facing page, centre right*).

Images of cerebral slices made at two different levels, after injection of ^{11}C-methionine in the same adult subject, on a normal diet (above) and after a loading dose of phenylalanine (below). One can see in the latter case a considerable diminution of cerebral fixation of ^{11}C-methionine; it is fixed only in the scalp.

determine the metabolism of normal and neoplastic tissue, and by Dollery and West (1960) to explore pulmonary function. As an example of what this radionuclide allows us to obtain with the methods we have at our disposal today, I will describe the technique used at the Service Hospitalier Frédéric Joliot for the study of cerebral blood flow and the extraction rate of oxygen using the method of continuous inhalation of $^{15}O_2$ and $C^{15}O_2$. This method, proposed by Jones *et al.* (1976), is based on a model of cerebral metabolism of ^{15}O in a steady state, as shown in Fig. 1. In the process of continuous inhalation of $C^{15}O_2$ there is an immediate exchange of ^{15}O between the $C^{15}O_2$ and pulmonary water. The water so labelled is distributed in the tissue according to the blood flow. Mathematical analysis of the model shows that the relation between activity in the stationary state and tissue blood flow is not linear. It depends, as shown in Fig. 2, on the physical half-life of the tracer used. We see that for values less than 50 ml per min per 100 g the flow can be measured with rather good precision, but that at higher values small variations in activity correspond to important differences in flow. For values greater than 100 ml per min per 100 g, corresponding to the upper physiological level in the case of cerebral tissue, the activity is independent of flow and essentially proportional to the dilution volume of the tracer.

In the course of inhalation of ^{15}O the tracer is fixed to the haemoglobin to be followed by extraction in the tissue of the Hb $^{15}O_2$ thus formed. The extracted oxygen is converted into intracellular $H_2{}^{15}O$ which exchanges with the plasma water (Fig. 1). Mathematical analysis of the model shows that in this case radioactivity in the stationary state depends both on the blood flow and on the coefficient of extraction of oxygen by tissue. It also shows that, in the stationary state, the ratio of the activities obtained in the course of inhalation of $^{15}O_2$ and $C^{15}O_2$ is equal to a factor close to the coefficient of extraction of oxygen by tissue. Figure 3 shows tomographic slices of the brain obtained by the ECAT. The upper part of the figure shows in a normal subject from left to right images of a brain slice obtained by $C^{15}O_2$ inhalation, then by $^{15}O_2$ inhalation and finally the ratio of the two images. Among these images, where the clearer tints correspond to the highest activities, the first represents the cerebral blood flow distribution; the second, the superposition of this distribution on the oxygen tissue uptake; and the third, the distribution of oxygen extraction. The two first are symmetrical and the third uniform, showing that in a normal subject oxygen extraction is homogeneous in all the cerebral tissue. The lower part of the figure shows the same images in a subject suffering from a recent infarct of the right sylvian region. The first image is clearly asymmetrical, displaying the hyperperfusion, an increase of blood flow in the lesion, well known to surgeons. The second image is also asymmetrical showing, on the contrary, a decrease in radioactivity in the lesion. The third image shows a large decrease in the oxygen extraction rate in the area of infarct. Baron *et al.* (1978) used this technique extensively and have shown that in infarcts evolving for more than 30 days, cerebral blood flow was always clearly lessened, whereas the oxygen extraction rate was more often normal. In recent infarcts three cases seem to appear:

- lessened oxygen extraction rate with reduced, normal or increased cerebral blood flow; this picture suggests tissue necrosis;
- increased oxygen extraction rate with decrease of cerebral blood flow, which seems to indicate a favourable tissue prognosis;
- normal oxygen extraction rate associated with an increase (good prognosis) or a decrease (poor prognosis) in cerebral blood flow.

One can thus see how this completely harmless method allows us to consider cerebral infarct physiopathology in a completely new light.

For such uses ^{15}O is produced by bombarding a nitrogen gas target with 7 MeV deuterons following the nuclear reaction ^{14}N (*d,n*) ^{15}O. The gas is then directed toward two circuits ending respectively in the production of $^{15}O_2$ and $C^{15}O_2$, which run out in a continuous flow in a 30 m long shielded pipe at the end of which is located the inhalation apparatus. Figure 4 schematizes this device.

USE OF NITROGEN 13

The synthesis time of molecules labelled with nitrogen in general exceeds the half-life of this radionuclide. Moreover, the yield of organic syntheses very rapidly decreases depending on the time needed to produce them. The activity of ^{13}N which can be obtained during production is not very high. Consequently, when we try to reduce the synthesis time in order to adapt it to the ten minute half-life, the labelling yield becomes negligible. Some amino acids have been labelled using rapid enzymatic synthesis which consists of introducing an amino function

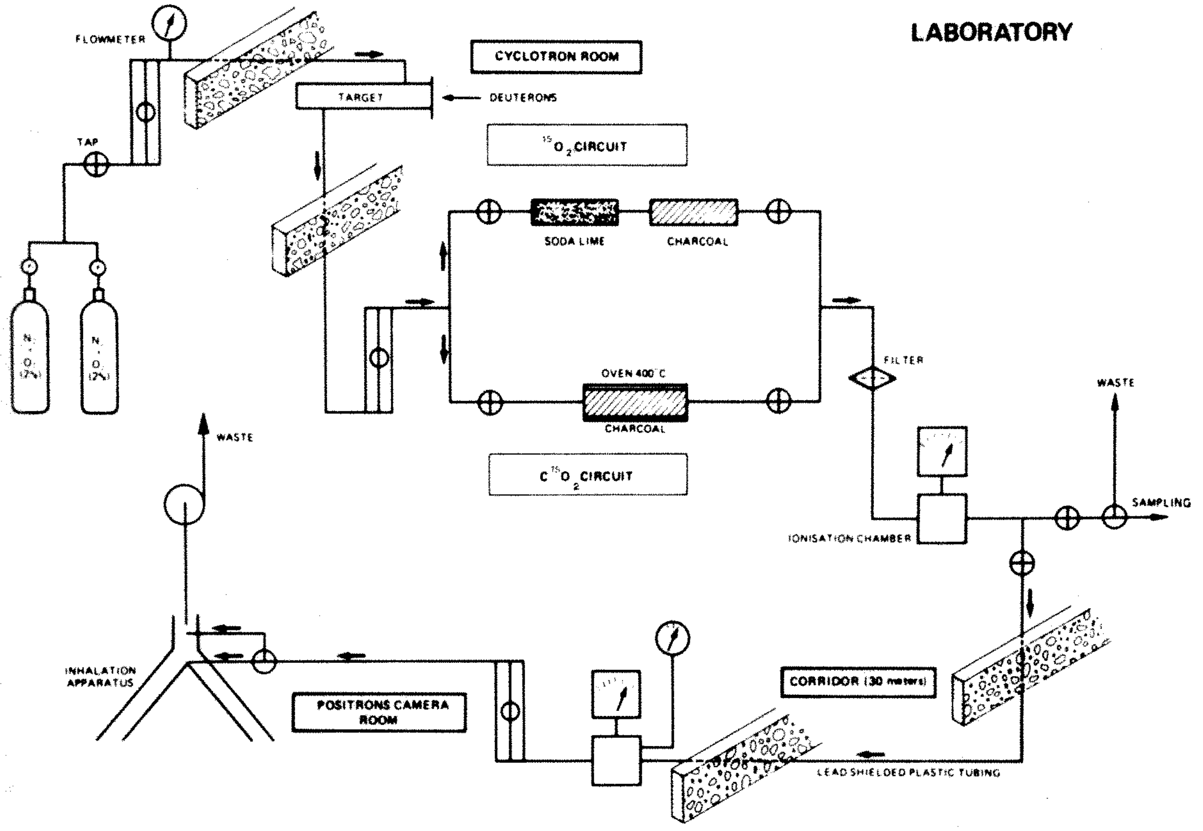


FIG. 4.

Scheme for the continuous production and utilization of $C^{15}O_2$ and $^{15}O_2$.

starting from $^{13}NH_4OH$ as precursor. L-glutamine, L-glutamic acid and L-asparagine were labelled in this way by Gelbard *et al.* (1974; 1975).

Nitrogen 13 gas has been used to study the distribution of pulmonary blood flow and ventilation by West (1968).

USE OF CARBON 11

The situation is quite different for ^{11}C. First, the reaction has a high yield of 75 MBq (2000 μCi)/μA min as shown in Fig.5 which represents the method used in producing $^{11}CO_2$, one of the main precursors needed for the synthesis of molecules labelled with ^{11}C. For an irradiation of about one half-life of ^{11}C, *i.e.* 20 minutes, with a proton current of 30 μA which is easy to obtain, the activity of the ^{11}C produced is of the order of 40 GBq (1 Ci). A number of organic synthesis methods can then be used during a period of time limited to one hour, *i.e.* three half-lives of ^{11}C. Despite poor yield, the molecule produced has an activity which is high enough to be used, considering the very high initial activity.

1. *Preparation of radiopharmaceuticals starting from ^{11}C*

The constraints imposed on the radiochemist are as follows: the preparation time should not exceed two to three half-lives of the radioelement used (it comprises the time for the synthesis as such, purification, generation of the radiopharmaceutical and quality control); the amount of radioactivity manipulated is high (of the order of 30 GBq) and, owing to the high energy of the emitted radiation (511 keV γ), radioprotection of the staff requires lead-shielded "production cells" with manipulation by remote control.

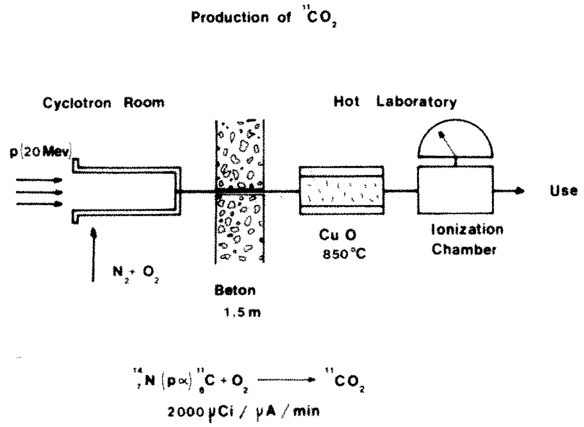


FIG. 5.
Production of $^{11}CO_2$.

(a) *Synthesis includes three methods*

(i) *Biological method.* The classic example is that of the photosynthesis of sugars starting from $^{11}CO_2$ according to the pioneer work of Lifton and Welch (1971). The process of incorporation is rapid and leads directly to D-glucose. However, there is still a problem with purification. The glucose must be separated from fructose which has also been labelled, and from pigments and proteins which—even in low concentration—may induce thermal shock and must be completely eliminated.

(ii) *Enzymatic method.* Starting from ^{11}C, pyruvic and lactic acids, L-alanine, L-glycine, hippuric and benzoic acids have all been labelled by the enzymatic route. In addition, we know how to synthesize "active" methionine (S-adenosyl methionine) with a labelled methyl group, and by enzymatic reaction to proceed by transmethylation to hormones such as adrenalin, or various derivatives of neurotransmitters (methoxydopamine, methoxy- or methyl- serotonin). The immobilization of enzymes on a base medium should permit the development of automatic rapid labelling of optically active derivatives.

(iii) *Organic synthesis.* Several ^{11}C labelled precursors such as formol (Berger *et al.*, 1980), methyl iodide (Marazano *et al.*, 1977), hydrocyanic acid (Straatman and Welch, 1975), phosgene (Roeda *et al.*, 1978) are at present available which provide

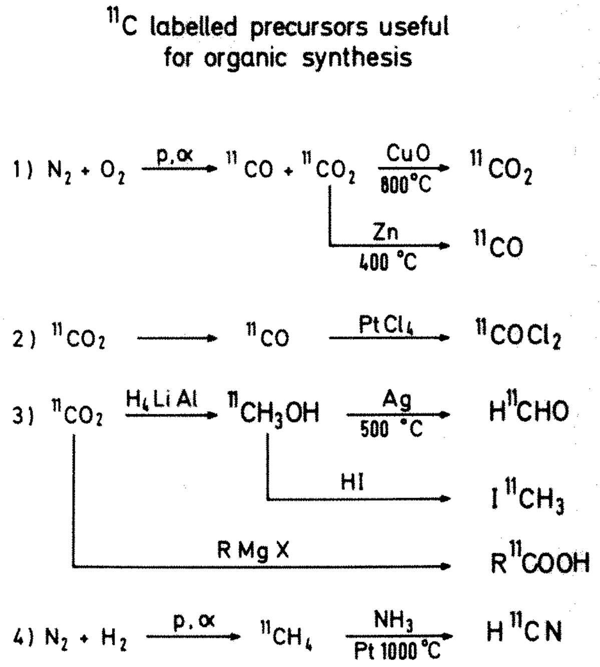

11C labelled precursors useful for organic synthesis
1) N2 + O2 —p,α→ 11CO + 11CO2 —CuO 800°C→ 11CO2
—Zn 400 °C→ 11CO
2) 11CO2 → 11CO —PtCl4→ 11COCl2
3) 11CO2 —H4LiAl→ 11CH3OH —Ag 500 °C→ H11CHO
—HI→ I11CH3
—R Mg X→ R11COOH
4) N2 + H2 —p,α→ 11CH4 —NH3 Pt 1000 °C→ H11CN

FIG. 6.
Methods of production of the principal precursors utilized for the labelling of molecules with ^{11}C by organic synthesis.

access to many natural molecules and drugs. Figure 6 summarizes these precursor production modes.

The labelling of the amino-acid carboxyl group can be performed, starting from $H^{11}CN$, to provide the racemic derivative. By this means DL-dopa (Reiffers *et al.*, 1977), DL-phenylalanine (Vaalburg *et al.*, 1976) and DL-valine (Washburn *et al.*, 1978), have been labelled. In addition, starting from $H^{11}CN$, various nitriles, amines and sugars (in particular 2-deoxyglucose) have been labelled. Starting from $^{11}CO_2$ and an organic magnesium precursor, the carboxy group of various fatty acids may be labelled.

Phosgene ^{11}C easily leads to urea, which itself is the starting point for barbiturates, hydantoines, etc.

A large number of molecules possessing a methyl group on an amino function may easily be labelled using the precursor ^{11}C-formaldehyde or methyl ^{11}C iodide. Such a method has been used for labelling L-methionine, various psychoactive neuroleptics, antidepressants, tranquillizers, derivatives of neurotransmitters, and alkaloids (Berger *et al.*, 1979). This by no means comprehensive list is given to show the great variety of molecules which one could envisage labelling despite the time constraint imposed. As an example, Fig. 7 summarizes the synthesis of C^{11}-chlorpromazine.

(b) *Purification*

The mass of material produced during a synthesis is in general very small, and as a result it is not possible to purify by crystallization. The high-pressure liquid chromatographic techniques (HPLC) recently developed are well suited for the task of purifying such reaction mixtures since they associate great speed with a high degree of purification. In addition, they may readily be performed automatically under remote control. Continuous recording of the radioactivity and concentration of the labelled product permits instantaneous measurement of the specific activity and purity of the product.

(c) *Preparation for use as a radiopharmaceutical*

This last step generally consists of the preparation of an injectable solution of the labelled product (controlling the sterility, pyrogenicity, pH and isotonicity). Given the short time available for performing these operations, it is almost impossible to perform all the checks recommended for injectable solutions.

In fact, the required checks are performed during "dummy runs" performed under standardized conditions within an extremely precise protocol which is then followed exactly if the tests and checks prove satisfactory. This procedure, which is the only method possible in the absence of techniques for rapid control (no more than several minutes), could present serious legal problems in the future.

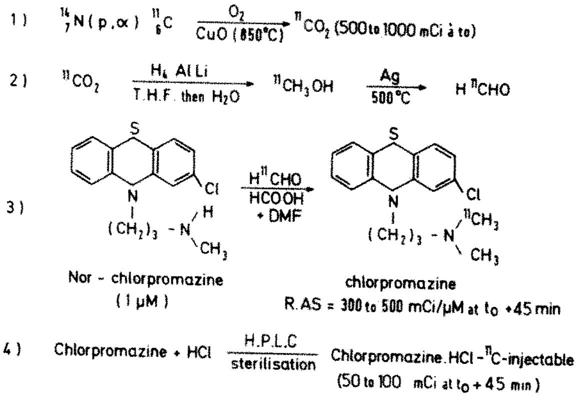

1)
$^{14}_{7}N(p,\alpha)\ ^{11}_{6}C \xrightarrow[CuO\ (850°C)]{O_2} {}^{11}CO_2$ (500 to 1000 mCi à to)
2)
$^{11}CO_2 \xrightarrow[T.H.F.\ then\ H_2O]{H_4AlLi} {}^{11}CH_3OH \xrightarrow[500°C]{Ag} H^{11}CHO$
3)
S
N
Cl
$(CH_2)_3-N$
H
CH_3
$H^{11}CHO$
HCOOH
+ DMF
$^{11}CH_3$
Nor - chlorpromazine
(1 μM)
chlorpromazine
R.AS = 300 to 500 mCi/μM at t_0 +45 min
4)
Chlorpromazine + HCl $\xrightarrow[sterilisation]{H.P.L.C}$ Chlorpromazine.HCl-^{11}C-injectable
(50 to 100 mCi at t_0 + 45 min)

FIG. 7.

The different stages of labelling of chlorpromazine chlorhydrate with ^{11}C.

2. *Some medical applications*

(a) ^{11}C *Methionine—pancreatic scanning with positron tomography* (Syrota *et al.*, 1979)

Compared with conventional scintigraphy using ^{75}Se-selenomethionine, the use of ^{11}C-methionine offers, in principle, some advantages.

(i) 500–700 MBq (15–20 mCi) may be injected without danger; the whole-body dose is about 1.8 mGy (180 mrad) after injection of 740 MBq (20mCi) of ^{11}C-methionine whereas it reaches 16 mGy after injection of 9MBq (250 μCi) of ^{75}Se-selenomethionine;

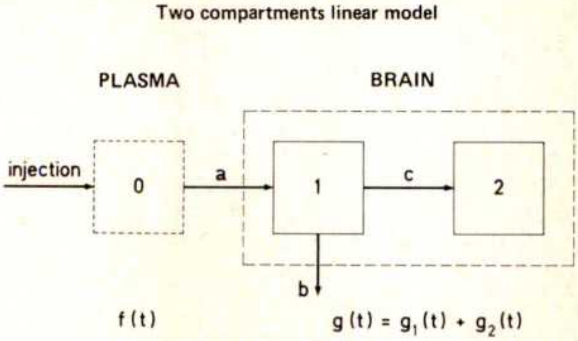
(ii) positron emission of ^{11}C allows transverse tomography.

Figure 8 shows, from a normal subject, five adjacent slices 2 cm thick, starting 4 cm above the umbilicus and proceeding upward. The head of the pancreas appears in the first two upper slices, from left to right, as a round or oval zone along the mid-line. The body of the pancreas appears in the third upper slices and the tail in the two last lower slices. Figure 9 represents four slices taken from a patient with cancer of the body of the pancreas. On the intermediate slice (upper right) corresponding to the body of the organ, the pancreas image has disappeared but it can be seen on the following slice in the lower left. Evidently the pancreas body did not take up methionine, and this indicates a lesion in the pancreas body, which in the present case turned out to be a cancer. Such results indicate the potential value of pancreatic study with ^{11}C-methionine and positron computed tomography, such as is available with transmission computed tomography and ultrasound, but it also provides functional information since it reflects uptake and incorporation of L-methionine in proteins.

(b) *Brain metabolism of carbon-11 methionine* (Comar *et al.*, 1980)

Methionine is one of the amino acids easily penetrating into the brain through the brain-blood barrier. In the congenital disease phenylketonuria, due to enzymatic defect in the transformation of phenylalanine into tyrosine, we observe an accumulation of phenylalanine in the blood, and irreversible mental retardation sets in rapidly during the months following birth. If a child afflicted with such a metabolic defect is subject, from birth until four or five years of age, to a diet not containing phenylalanine, mental retardation does not apparently develop. In order to understand better the brain metabolism of amino acids and eventually to evaluate more accurately the minimum treatment time necessary, the use of ^{11}C methionine as an indicator of permeability of the brain-blood barrier seems indicated. We know that an excess of blood phenylalanine inhibits the passage of several other indispensable amino acids, including methionine, into the brain of rats. The intensity of this phenomenon is greater as the concentration of blood phenylalanine is higher. This phenomenon is illustrated by the curves in Fig. 10 and the corresponding conventional scintigraphic images. The full line was obtained from a child on a diet without phenylalanine, consequently with a low blood level of these amino acids. This full-line curve, as well as the scintigraphic images, shows clear brain uptake of methionine. The dotted line shows a decrease in uptake of methionine to such an extent that this uptake is not perceptible on the scintigram. The difference observed between the two tests is quite important and clearly indicates the inhibition in the brain penetration of methionine during this disease.

This result is confirmed by brain tomographic images, taken with ECAT and represented on Fig. 11. The upper images correspond to two slices taken at different levels in a normal patient. The lower images correspond to the same two slices taken in the same patient after overloading the blood with phenylalanine. We can see that the excess of these amino acids in the blood inhibits the passage of labelled methionine through the brain-blood barrier. We should note, however, that there is no modification in the uptake of methionine in the scalp. Figure 12 corresponds to an attempt to model brain methionine kinetics. In this compartmental representation, compartment 0 may correspond to the free methionine in the plasma, compartment 1 to the free methionine in the brain, and compartment 2 to the methionine of brain protein. For such a model, plasma and brain activities of ^{11}C methionine determine the transfer rates *a*, *b* and *c*. To the extent that the physiological interpretation of such a model is correct, the determination of the transfer rate *c* should correspond to the synthesis rate of brain protein.



$$g(t) = g_1(t) + g_2(t)$$

$$\begin{cases} \dfrac{dg_1}{dt} = af - (b+c)\,g_1 \\ \dfrac{dg_2}{dt} = cg_1 \end{cases}$$

FIG. 12.
Compartment model of the cerebral kinetics of methionine.

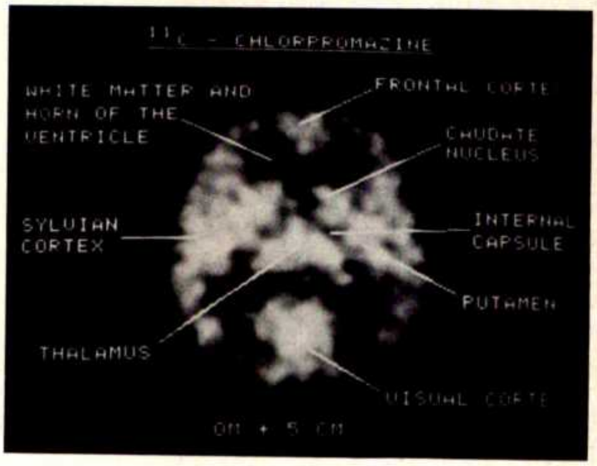


FIG. 13.
Distribution of ^{11}C-chlorpromazine in the human brain.

(c) In vivo *visualization of neuro-receptors in man*

(i) *Chlorpromazine*

The distribution of chlorpromazine in the brain was studied for this purpose after labelling it with ^{11}C on the methyl group present at the end of the side chain of the molecule (Comar *et al.*, 1979a).

Specific activities as high as 20 GBq (500 mCi)/μmol were obtained, and hence injection of a test dose of 350–700 MBq (10–20 mCi) resulted in the injection of 20–40 nmol of cold chlorpromazine, far below a therapeutic dose. The typical pattern of brain distribution of chlorpromazine is shown in Fig. 13. The relatively homogeneous distribution of the labelled drug in the grey matter prevents direct observation of specific receptor binding. Because of the very fast initial uptake and subsequent slower increase of radioactivity, which point to a high blood-brain permeability and slow cerebral metabolism within the time scale of the examination, we tend to interpret these images in terms of cerebral blood-flow distribution. Possible binding to a specific dopaminergic or noradrenergic receptor cannot be visualized in these images owing to very high uptake of the drug by non-specific sites which cannot be differentiated from the specific sites because of the low spatial resolution of the detection device.

(ii) *Benzodiazepine*

Recently, specific binding of benzodiazepines (diazepam and flunitrazepam) was demonstrated in the brain of animals *in vitro*. Accordingly, we have attempted to determine if this binding can be observed *in vivo* (Comar *et al.*, 1979b). Flunitrazepam was labelled with ^{11}C at a specific activity of 20–30 GBq (500–800 Ci)/μmol. The labelled drug (800 MBq (20–25 mCi), corresponding to 2–6 nM per kg), was injected intravenously into baboons (*Papio papio*). The distribution kinetics of the radiopharmaceutical were followed by positron emission tomography. At a given time after injection of the radioactive ligand, lorazepam at micromolar concentration was injected in order to displace the radioactivity from the specific binding sites. This displacement is shown in the

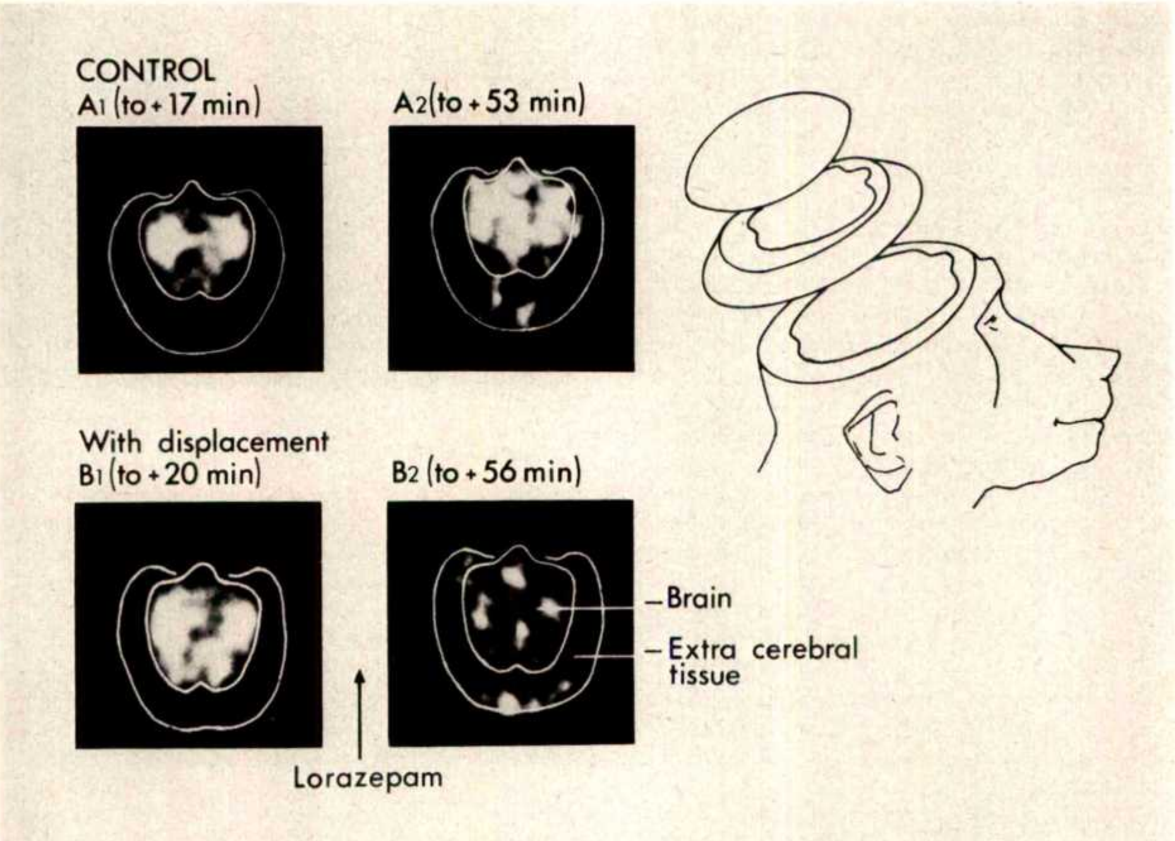


FIG. 14.

Cerebral distribution of ^{11}C-flunitrazapam observed at the different times after intravenous injection in the baboon (*Papio papio*). A_1 and A_2 are control animals. Image B_1 was obtained before administration of lorazepam; B_2 was obtained 26 min after injection of lorazepam 20 min after the injection of ^{11}C-flunitrazapam.

images of Fig. 14 which show brain distributions in the baboon at different times after i.v. injection of ^{11}C-flunitrazepam observed by positron emission tomography. Comparison of B2 (obtained 26 min after administration of 1.3 μM/kg of lorazepam), with A2 (control) reveals a displacement of the radioactive ligand. Figure 15 shows the mean displacement effect for eight animals, which is highly significant.

Lorazepam, another benzodiazepine, was used for this displacement study because of its high affinity for the receptors. This experiment was conducted under conditions that could be reproduced in humans, thus providing the possibility of studying directly the mechanism of how drugs act, and evaluating specific brain receptor localization and density in various pathological situations. Analysis of brain tissue samples taken after death has shown that dopamine receptors in the caudate nucleus were decreased in Parkinson's disease and increased in schizophrenia and that benzodiazepine receptors were either increased or decreased according to the the tissues studied in Huntington's disease. Such observations *in vitro* have encouraged us to pursue the development of *in vivo* methods.

CONCLUSION

The use of molecules labelled with ^{11}C for metabolic explorations in man involves an extremely ponderous procedure. The cyclotron itself is not a major problem, except financially. One can have at one's disposal today a machine whose operation presents no greater difficulties than those of a linear accelerator or a betatron of the kind used in radiotherapy.

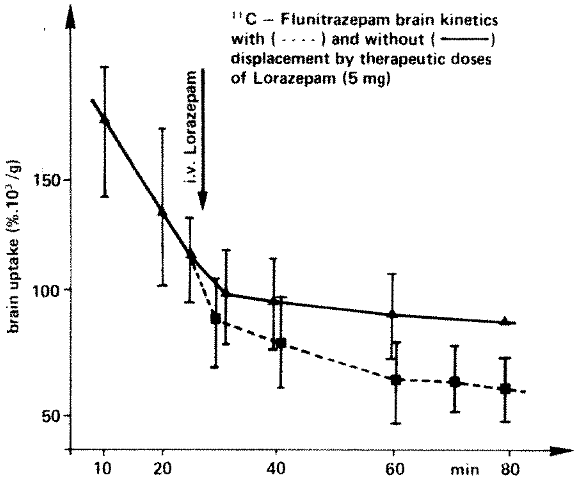


FIG. 15.

Cerebral kinetics of ^{11}C-flunitrazapam with and without displacement with lorazepam.

On the other hand, the apparatus for detecting and visualizing annihilation radiation is still quite imperfect. Its sensitivity is insufficient to follow the kinetics of rapid metabolic processes and its spatial resolution needs to be improved. In addition, an important problem which is still not resolved is that of making quantitative measurements.

But, to my mind, the chief limitations involve the chemistry. There we face a multitude of problems:

the radioactivity manipulated by the chemist must be considerable because of poor synthesis yields resulting from the short lifetime of ^{11}C;

for purposes of protection of personnel, the synthesis of each molecule should be entirely automatic, which is a difficult and onerous task;

the chemistry deals with virtually weightless quantities of material for which the usual rules do not apply and the phenomena of adsorption play a large role;

finally, since carbon is an element widely found in nature, the specific radioactivities which one can obtain are much lower than that which is theoretically possible.

It will probably be difficult to obtain high enough specific activities to resolve certain problems, such as the visualization of receptor sites of hormones or drugs.

Finally, because of the short life of ^{11}C it is necessary to make an entire synthesis for only one, or at best two examinations. The number of examinations made each day is very limited. Thus, even though the association of cyclotron, chemistry, camera and ^{11}C is a powerful research tool, I do not think that under present conditions it can be used for routine clinical work. Nevertheless, the method described is the only one which permits the study of metabolic processes in man by non-invasive procedures; I therefore believe that all efforts should be undertaken to improve it.

REFERENCES

ANGER, H. O., 1958. Scintillation camera. *Review of Scientific Instruments, 29*, 27–33.

BARON, J. C., COMAR, D., BOUSSER, M. G., SOUSSALINE, F., CROUZEL, C., PLUMMER, D., KELLERSHOHN, C. and CASTAIGNE, P., 1978. Etude tomographique, chez l'homme, du débit sanguin et de la consommation d'oxygène du cerveau par inhalation continue d'oxygène 15. *Revue Neurologique, 134*, 545–556.

BERGER, G., MAZIERE, M., KNIPPER, R., PRENANT, C. and COMAR, D., 1979. Automated synthesis of ^{11}C labelled radiopharmaceutical: Imipramine, Chlorpromazine, Nicotine and Methionine. *International Journal of Applied Radiation and Isotopes, 30*, 393–399.

BERGER, G., MAZIERE, M., SASTRE, J. and COMAR, D., 1980. Carrier-free ^{11}C formaldehyde: an approach. *Journal of Labelled Compounds and Radiopharmaceuticals, 27*, 59–71.

BROWNELL, G. L. and BURNHAM, C. A., 1973. MGH positron camera. In *Tomographic Imaging in Nuclear Medicine,* Ed. G. S. Freedman (Society of Nuclear Medicine, New York), pp. 154–164.

Cassen, B., Curtiss, L., Reed, C. and Libby, R., 1951. Instrumentation of I^{131} used in medical studies. *Nucleonics, 9*, 46.

Comar, D., Zarifian, E., Verhas, M., Soussaline, F. Maziere, M., Berger, G., Loo, H., Cuche, H., Kellershohn, C. and Deniker, P., 1979a. Brain distribution and kinetics of ^{11}C-chlorpromazine in schizophrenics: positron emission tomography studies. *Psychiatry Research, 1*, 23–29.

Comar, D., Maziere, M., Godot, J. M., Berger, G., Soussaline, F., Menini, Ch., Arfel, G. and Naquet, R., 1979b. Visualization of ^{11}C-flunitrazepam displacement in the brain of the live baboon. *Nature, 280*, 329–331.

Comar, D., Maziere, M., Saudubray, J. M., Zarifian, E. and Naquet, R., 1980. Positron emission tomography and cerebral metabolism. In *Computerized Tomography*, Eds. J. M. Caillé and G. Salmon (Springer-Verlag, Berlin/Heidelberg/New York), pp.224–230.

Cormack, A. M., 1963. Representation of a function by its line integrals, with some radiological applications. *Journal of Applied Physics, 34*, 2722–2727.

1964. Representation of a function by its line integrals, with some radiological applications II. *Journal of Applied Physics, 35*, 2908–2913.

Dollery, C. T. and West, J. B., 1960. Regional uptake of radioactive oxygen, carbon monoxide and carbon dioxide in the lungs of patients with mitral stenosis. *Circulation Research, 8*, 765–771.

Donald, I., 1976. New diagnostic horizons with sonar. *British Journal of Radiology, 49*, 306–315.

Gelbard, A. S., Clarke, L. R. and Laughlin, J. S., 1974. Enzymatic synthesis and use of ^{13}N-labelled L-asparagine for myocardial imaging. *Journal of Nuclear Medicine*, 15, 1223–1225.

Gelbard, A. S., Clarke, L. R., McDonald, J. M., Monahan, W. G., Tilbury, R. S., Kuo, T. Y. T. and Laughlin, J. S., 1975. Enzymatic synthesis and organ distribution studies with ^{13}N-labelled L-glutamine and L-glutamic acid. *Radiology, 116*, 127–132.

Hamilton, J. G. and Soley, M. H., 1940. Studies in iodine metabolism of the thyroid gland *in situ* by use of radio-iodine in normal subject and in patients with various types of goitre. *American Journal of Physiology, 131*, 135–143.

Hevesy, G. Von, 1948. *Radioactive Indicators: Their Application in Biochemistry, Animal Physiology and Pathology* (Interscience, New York).

Hounsfield, G. N., 1973. Computerized transverse axial scanning (tomography): Part 1—Description of system. *British Journal of Radiology, 46*, 1016–1022.

Jones, T., Chesler, D. A. and Ter-Pogossian, M. M., 1976. The continuous inhalation of oxygen-15 for assessing regional oxygen extraction in the brain of man. *British Journal of Radiology, 49*, 339–343.

Lifton, J. F. and Welch, M., 1971. Preparation of glucose labelled with 20-minute half-lived carbon 11. *Radiation Research, 45*, 35–40.

Mackenzie Davidson, J., 1912. Vital effects of radium and other rays. *Proceedings of the Royal Institution of Great Britain, 20*, (106), 291–308.

Mackenzie Davidson, J. and Hedley, W. S., 1897. A method of precise localization and measurements by means of Roentgen rays. *Lancet, 2*, 1001.

Marazano, C., Maziere, M., Berger, G. and Comar, D., 1977. Synthesis of methyliodide-^{11}C and formaldehyde-^{11}C. *International Journal of Applied Radiation and Isotopes, 28*, 49–52.

Mayneord, W. V. and Newbery, S. P., 1952. An automatic method of studying the distribution of activity in a source of ionizing radiation. *British Journal of Radiology*, 25, 589.

Newbery, G. R., 1959. Cyclotron produced isotopes in clinical and experimental medicine. *British Journal of Radiology, 32*, 633–641.

Phelps, M. E., Hoffman, E. J., Mullani, N. A. and Ter-Pogossian, M. M., 1975. Application of annihilation coincidence detection to transaxial reconstruction tomography. *Journal of Nuclear Medicine, 16*, 210–223.

Reiffers, S., Beerling-Van Der Molen, H. D., Vaalburg, W., Ten Hoeve, W., Paans, A. M. J., Korf, J., Woldring, M. G. and Wynberg, H., 1977. Rapid synthesis and purification of carbon-11 labelled DOPA: a potential agent for brain studies. *International Journal of Applied Radiation and Isotopes, 28*, 955–958.

Roeda, D., Crouzel, C. and Van Zanten, B., 1978. The production of ^{11}C-phosgene without added carrier. *Radiochemical Radioanalytical Letters, 33*, 175–178.

Straatman, M. G. and Welch, M. J., 1975. A general method for labelling proteins with ^{11}C. *Journal of Nuclear Medicine, 16*, 425–428.

Syrota, A., Comar, D., Cerf, M., Plummer, D., Maziere, M. and Kellershohn, C., 1979 [^{11}C] Methionine pancreatic scanning with positron emission computed tomography. *Journal of Nuclear Medicine, 20*, 778–781.

Ter-Pogossian, M. M., Mullani, M. A., Hood, J., Higgins, C. S. and Currie, M. C., 1978. A multislice positron emission computed tomograph (PETT IV) yielding transverse and longitudinal images. *Radiology, 128*, 477–484.

Ter-Pogossian, M. M. and Powers, W. E., 1958. The use of radioactive oxygen-15 in the determination of oxygen content in malignant neoplasms. In *Radioisotopes in Scientific Research, III*, Ed. R. C. Extermann (Pergamon Press, Oxford), pp. 625–636.

Vaalburg, W., Beerling-Van Der Molen, H. D., Reiffers, S., Rijskamp, A., Woldring, M. G. and Wynberg, H., 1976. Preparation of carbon-11 labelled phenylalanine and phenylglycine by a new amino acid synthesis. *International Journal of Applied Radiation and Isotopes, 27*, 153–157.

Washburn, G. C., Wiegand, B. W., Sun, T. T., Hayes, R. G. and Butler, T. A., 1978. 1-^{11}CDL-Valine, a potential pancreas-imaging agent. *Journal of Nuclear Medicine, 19*, 77–83.

West, J. B., 1968. Studies of pulmonary and cardiac function using short-lived isotopes oxygen-15, nitrogen-13 and carbon-11. In *Progress in Atomic Medicine, Nuclear Medicine and Recent Advances*, Ed. J. H. Lawrence (Grune and Stratton, New York), pp. 39–64.

Yamamoto, Y., Thompson, C. J. and Meyer, E., 1977. Dynamic positron emission tomography for study of cerebral hemodynamics in a cross-section of the head using positron emitting ^{68}Ga–EDTA and ^{77}Kr. *Journal of Computer Assisted Tomography, 1*, 43–56.

1981, *British Journal of Radiology*, 54, 103–109

The radiology of carcinoma of the ear

By P. D. Phelps, F.R.C.S., F.R.C.R. and G. A. S. Lloyd, D.M., F.R.C.R.

The Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London WC1X 8DA

(*Received September 1980*)

ABSTRACT

Carcinoma arising in external auditory meatus, middle ear cleft or mastoid cavity has a poor prognosis unless treated at an early stage. Biopsy of any suspicious tissue is the key to early diagnosis but there are radiological features which may suggest the presence of a malignant neoplasm. An important role of radiology is the demonstration of the extent of disease and of spread beyond the confines of the temporal bone. The optimum regime of surgery and radiotherapy cannot be planned without this information.

The radiological features of 47 aural carcinomas were reviewed. Thirty-two of the cases were examined by multidirectional tomography and six by computed tomography. The modes of spread of the neoplasm are discussed as well as the differential diagnosis. It is concluded that high resolution CT is now the optimum method of demonstrating tumour spread in the axial plane and frequently also in the coronal section. Lateral tomograms are necessary to show erosion of the walls of the external auditory meatus. Erosion of the bony septum separating the middle ear cavity from the carotid canal can be shown on coronal sections and is an important sign of spread anteriorly. Soft tissue extension into the infratemporal fossa may be demonstrated by high resolution CT.

Cancer of the ear, arising in the external auditory meatus, middle ear cleft or in a mastoid cavity, is a rare but distressing disease which is seldom diagnosed early. Lewis (1973) estimates an average period of time from initial symptoms to diagnosis of six months. Only about 10% of squamous carcinomas can be classified as early lesions, usually arising from the membranous external auditory meatus. He suggests that the classic features of bloody discharge and pain in fact indicate fairly advanced disease. The association of carcinoma of the ear with chronic suppurative otitis media is well recognized and variously estimated as occurring in 30% to 75% of cases (Maran and Jacobson, 1979; Zizmor and Noyek, 1969). The presence of a cholesteatoma has been described in a few cases (Lewis, 1973). Squamous carcinoma is by far the commonest malignant tumour of the ear but adenocarcinoma and adenoid cystic carcinoma occur rarely, as well as lymphoma, malignant melanoma and various sarcomas including rhabdomyosarcoma of childhood.

Carcinoma arising in the membranous auditory meatus tends to spread into the parotid gland and the post auricular sulcus, whereas a tumour arising from the deep bony meatus may perforate the eardrum at an early stage. It is therefore often impossible to assess the exact site of origin of the tumour or to decide whether it has arisen from the deep meatus or the middle ear cleft (Goodman, 1971). Treatment by various regimes of surgery and radiotherapy can give a 30% five-year salvage, depending on the site of origin and extent of the disease.

There have been few accounts of the radiological features of ear cancer. Chen and Dehner (1978) found X-ray evidence of initial bone destruction in only six of 24 cases of carcinoma of the external auditory meatus, while Lewis (1960) states that positive X-ray findings were present in only 50% of his patients at the time of biopsy. Of these 42 patients with cancer originating in the external ear canal 30% showed evidence of chronic mastoiditis, and in 12% a tumour and destruction of bone were present. The remaining 8% showed a previous mastoid defect and chronic inflammation. Of his 18 cases of cancer arising in the middle ear and mastoid bone, destruction was evident on X-ray examination in 40%; 50% showed pathological changes suggesting chronic inflammation; one had only a mastoid defect following surgery; and in one case the X-ray findings were negative.

During the last 20 years newer radiological techniques, particularly multidirectional tomography, arteriography and venography, have become available. More recently a great advance in soft tissue imaging has been made with computed tomography, and in the high resolution mode CT has been shown to have great value in demonstrating bone changes in the petrous temporal region (Lloyd *et al.*, 1980). An attempt to assess the value of these new techniques in the management of carcinoma of the ear seemed appropriate in the hope that they might help to give earlier diagnosis, and a better demonstration of the extent of this painful and distressing disease, leading to improved treatment planning.

MATERIAL AND METHODS

The clinical and radiological records of all cases of malignant neoplasia of the ear investigated at The Royal National Throat, Nose and Ear Hospital,

---

Address for reprints: Dr. P. D. Phelps, Department of Radiology, The Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London WC1X 8DA.

London and The Coventry and Warwickshire Hospital, Coventry during the last 25 years were examined. Carcinomas arising from the pinna, and in one case the tragus, were excluded even if the external auditory meatus became subsequently involved. The series is not representative of the incidence of cancer of the ear as many of the London patients were referred after preliminary diagnosis and treatment elsewhere. This has made it difficult or impossible to determine the precise origin of the tumours, although all were considered to have arisen in the external auditory meatus, middle ear cleft or in a mastoid cavity.

X-ray films of 38 patients were available, one of whom had bilateral squamous cell carcinoma of the middle ear. Of these 39 aural neoplasms, one was an adenoid cystic carcinoma, two were transitional cell carcinomas, one was an anaplastic lesion of uncertain type and 35 were squamous cell carcinomas with various degrees of differentiation. The patients were examined by plain mastoid and temporal bone radiographs. Hypocycloidal tomograms in the coronal plane were obtained for 32 ears, lateral tomograms in the sagittal plane for 17. CT scans, mostly in the coronal as well as the axial plane and using the high resolution mode, were available for six patients.

The clinical records and radiological reports, but not the films, were available for a further eight patients, with seven squamous cell and one anaplastic carcinoma. These eight patients from the early years of this survey had only a plain film radiographic examination, and judging by the reports, mostly had extensive bone destruction with similar features to other advanced lesions in the series.

Careful assessment was made of the more subtle aspects of bone erosion in the petromastoid and tympanic bones as shown by plain films, tomograms and CT. Evidence of soft tissue extension of the neoplasm upwards and backwards into the cranial cavity, and downwards and forwards into the infratemporal fossa was looked for on the CT scans.

RESULTS

There was a history of long term otorrhoea and chronic ear infection for a period of more than one year in 17 cases. Eight of the patients had had previous mastoidectomies and the growth appeared on exploration to have arisen in the resultant cavity. Cholesteatoma was found as well as tumour in three cases, none of whom had had previous surgery. Twenty-five patients had symptoms for one year or less. The presenting features were pain, otorrhoea often blood-stained, facial palsy and deafness, as well as swelling in the vicinity of the external meatus and the presence of "polyps" or "papillomas" in the meatus. For four patients clinical records were inadequate. One patient who presented with a malignant polyp in the external auditory meatus developed a facial palsy and a mass in the neck soon afterwards. Computed tomography, besides showing erosion of the floor of the external meatus and middle ear, also outlined the large mass in the infratemporal fossa, bulging the wall of the post-nasal space (Fig. 1). The lesion was a rapidly growing anaplastic carcinoma which could have arisen in external auditory meatus, middle ear, parotid gland or even the post-nasal space. It is included in this series as the initial presentation was as an aural polyp.

In most cases in this series, the carcinoma appeared to have arisen in the external auditory meatus, although the presence of a normal middle ear and intact eardrum at surgery, or a normal air containing middle ear on tomography could be confirmed in only nine cases. Four of these had normal well-pneumatized mastoids. Not surprisingly the response to treatment was better in these nine patients than in the remaining 37 where the middle ear was involved. The most important radiological sign suggesting a diagnosis of carcinoma was erosion of the walls of the bony external auditory meatus (Fig. 2). This was

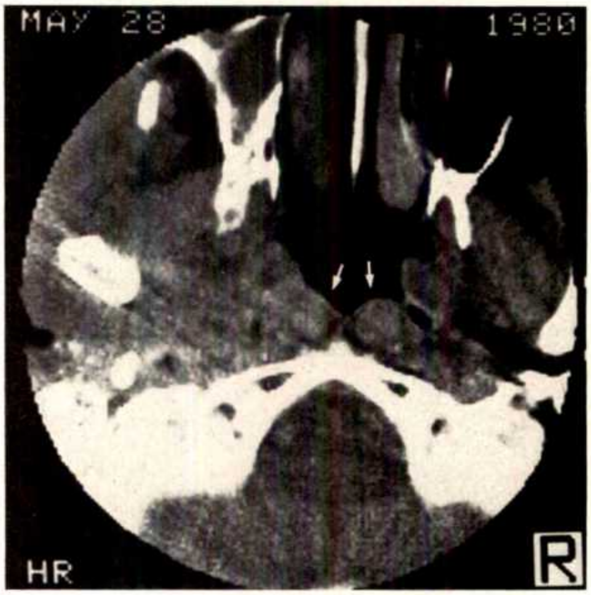


FIG. 1.

Carcinoma of the ear with spread anteriorly. Axial high resolution CT scan. The mass is bulging into the left side of the post-nasal space and has obliterated soft tissue detail in the left infratemporal fossa. Note the enlarged retropharyngeal lymph nodes (arrows).

best shown by lateral tomography and axial CT. Soft tissue extension forward from the external meatus was not so reliably demonstrated by axial CT.

Where the middle ear or mastoid was involved the middle ear cavity was always opaque and the mastoid usually but not always sclerotic. Bone erosion was the most important sign of carcinoma, and was different from that produced by acquired cholesteatoma. Where coronal section tomography was used, the outer attic wall or spur was shown to be deficient in only seven of the 32 ears with carcinoma, but four of these had had previous mastoidectomies, one had an associated cholesteatoma and the other two had extensive erosion of the superior aspect of the external auditory meatus. In no case did erosion of the spur appear as an early sign. Similarly destruction of the ossicles was only noted in two cases with extensive disease but in three others there was some displacement (Fig. 3). In only one case was erosion of the bony labyrinth observed, and this was associated with extensive destruction of the skull base (Fig. 4). Although there was no radiological evidence of direct invasion of the inner ear from the middle ear cleft, five patients had a dead ear at the time of the examination.

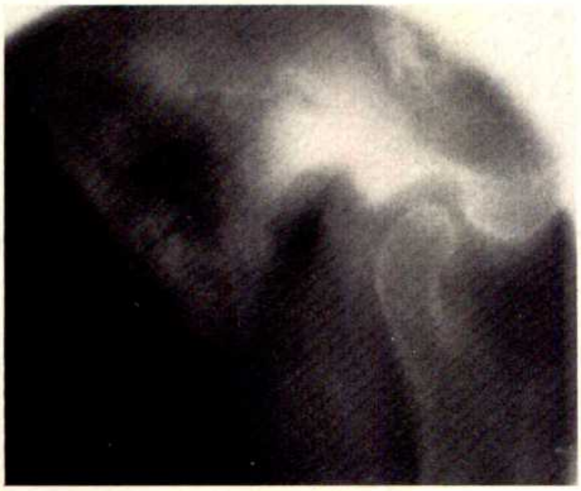


FIG. 2.

Lateral tomogram showing soft tissue swelling in the external auditory meatus with erosion of the anterior and inferior walls and extension into the temporo-mandibular joint. Note the well pneumatized mastoid process.

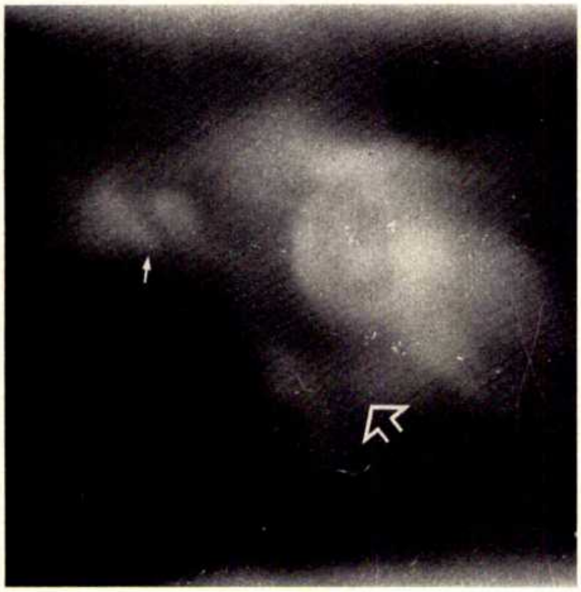


FIG. 3.

Coronal tomographic section at the level of the cochlea. There is extension of the carcinoma anteriorly down the axis of the Eustachian tube which is widened (open arrow). The septum separating the intrapetrous carotid from the middle ear has been destroyed. There is a soft tissue mass in the middle ear and the malleus is displaced laterally, but both this and the "spur" (small arrow) are intact.

Erosion in an anterior direction from the middle ear cavity was shown in eight of the cases who had tomograms and CT. Three of these had extensive erosion of the base of the middle cranial fossa, one had limited erosion in the region of the foramen lacerum, and four showed erosion limited to the thin bony septum which separates the middle ear cavity from the carotid canal (Fig. 5). One of these cases died from carotid haemorrhage two months after the radiological examination and another was noted to have extension of disease "beyond the carotid canal" at a subsequent petrosectomy operation (Fig. 6). Computed tomography was surprisingly good at demonstrating soft tissue extension of the tumour down the axis of the Eustachian tube and into the infratemporal fossa (Fig. 7). The findings in the six cases who had a CT examination are summarized in Table I.

Neoplastic invasion of the mastoid region with or without a previous mastoid cavity was suggested in a few cases by ragged erosion more extensive than would be expected with chronic infection. In one case high resolution CT showed a breach in the posterior surface of the petrous pyramid suggesting extension into the cranial cavity (Fig. 8). In no case however did CT demonstrate an abnormal soft tissue mass in the middle or posterior cranial fossa. Neither retrograde jugular venography nor carotid angiography was performed on any of these patients.

DISCUSSION

Carcinoma of the middle ear, external meatus or mastoid is a rare disease, few centres seeing an average of more than one case a year. Metastatic

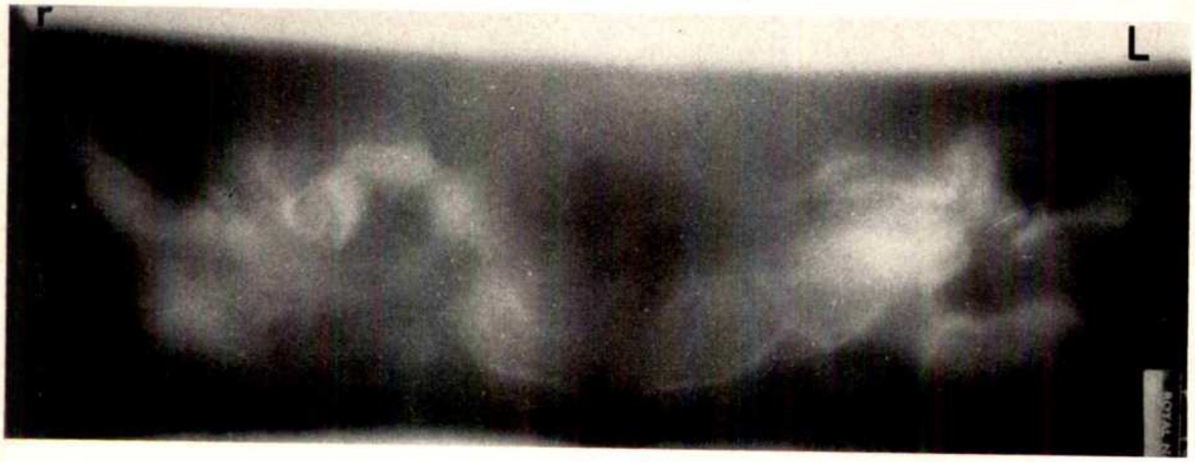


FIG. 4.

Coronal tomographic section at the level of the cochlea. Extensive erosion of the skull base on the right. Most of the cochlea has been preserved and the malleus can be identified.

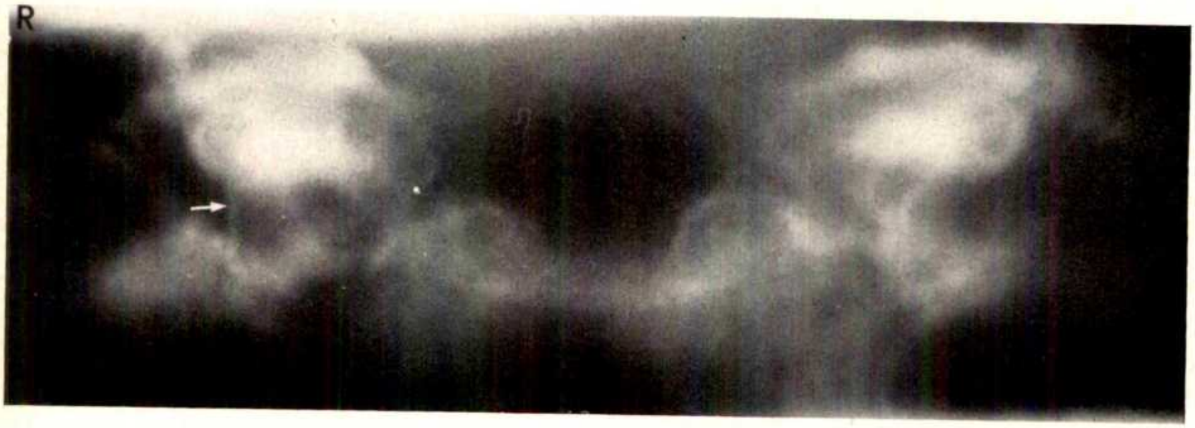


FIG. 5.

Coronal tomographic section at the level of the cochlea. The arrow shows the thin bony septum that separates the middle ear cavity from the carotid canal. On the left side the septum has been eroded by a middle ear carcinoma.

spread is unusual and the patients die in great pain from local infiltration and extension of the disease. Early diagnosis depends on a high index of suspicion leading to biopsy of polyps or "granulation tissue" in the middle ear or external meatus. The diagnosis of carcinoma in the mastoid is usually made while performing a mastoidectomy in an effort to control presumed chronic mastoiditis (Clairmont and Conley, 1977).

There was a history of chronic ear infection and otorrhoea of more than one year's duration in only 40% of our cases, but otorrhoea and signs of infection were unusual at the time of presentation. Sclerosis of the mastoid and clouding of the cells are therefore radiological signs of little value, but the presence of ragged erosion, usually extensive or in an unusual site, suggests neoplastic change (Fig. 9). An important sign on the lateral mastoid view is erosion of the articular fossa of the temporo-mandibular joint. This was present on the initial radiographs in 30% of our cases. Much better demonstration of erosion of the bony external auditory meatus and back of the temporo-mandibular joint was given by lateral tomograms (Fig. 2), and we consider this an obligatory investigation when carcinoma of the ear is suspected. Minor erosions will indicate the site for further exploration and biopsy, if the initial biopsies prove negative.

Diseases which may have a similar radiological appearance to squamous cell carcinoma of the ear are tuberculous otitis media, where there may be extensive bone destruction, and malignant otitis externa.

TABLE I

RADIOLOGICAL FINDINGS IN THE SIX CASES OF EAR CANCER INVESTIGATED BY CT

Probable site of origin	Plain films and multidirectional tomography	CT	Comments
EAM	Erosion of anterior wall of EAM best shown on lateral tomograms	Erosion of anterior wall of EAM	Evidence of soft tissue extension inconclusive
EAM	Soft tissue mass in EAM—nothing else. Lateral tomograms not done	Soft tissue mass in EAM ME air-containing	Infiltration into parotid from EAM not shown
EAM	EAM eroded anterior and inferior. Carotid canal septum eroded	Erosion of anterior wall of EAM; carotid septum and post surface of pyramid eroded	Anterior and posterior extension only fully demonstrated by axial CT
EAM	No abnormality shown	Mass in EAM. ME air-containing	Limited disease
ME	Erosion of base of skull in region of foramen lacerum	Extent of erosion better shown Soft tissue mass in infratemporal fossa	Axial CT gave best overall demonstration
ME	Erosion of base of skull and floor of EAM and ME	Soft tissue mass in infratemporal fossa	Extension of mass to the post nasal space a surprise finding on axial CT

EAM = external auditory meatus. ME = middle ear cavity.

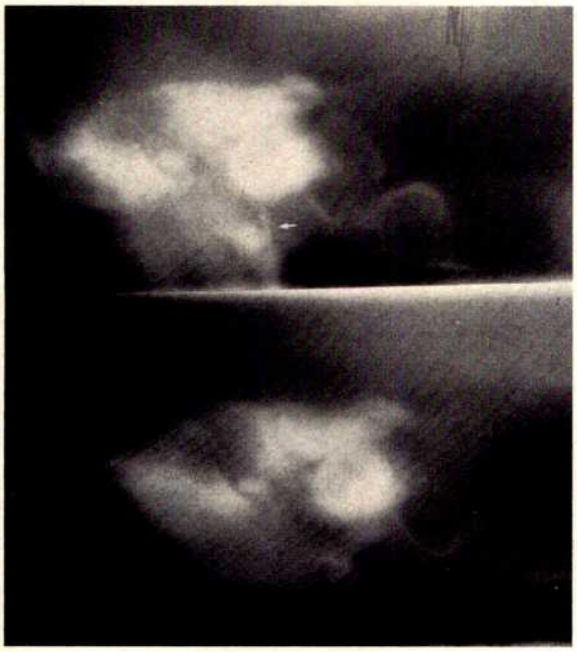


FIG. 6.

Two equivalent coronal sections at the level of the cochlea, but taken five months apart. The upper print shows an intact carotid septum (arrow), which can no longer be demonstrated on the later section. Extension of disease beyond the carotid canal was subsequently confirmed at surgery.

This non-neoplastic condition almost always occurs in elderly diabetics. Endarteritis and superadded infection lead to extensive destruction of the external auditory meatus, temporo-mandibular joint and middle ear making radiological differentiation from carcinoma difficult (Kim, 1971). Glomus tumours also cause ragged erosion of the skull base but the involvement of the margins of the jugular fossa, a late feature with carcinoma or malignant otitis, will suggest the correct diagnosis.

The hard avascular bone of the labyrinthine capsule is relatively unaffected by carcinoma of the ear, and erosion of the capsule with direct invasion of the inner ear is a late radiological feature, only present with extensive surrounding bone destruction. Michaels and Wells (1980) have shown by means of serially sectioned temporal bones that there are two important modes of spread of carcinoma of the middle ear (Fig. 10). Firstly the tumour extends anteriorly and penetrates the bony septum separating the middle ear cavity from the carotid artery. It then spreads around the artery, and extends down around the Eustachian tube towards the post-nasal space. Erosion of the carotid septum (Fig. 5), margins of the bony Eustachian tube (Fig. 4), and even soft tissue extension of the tumour anteriorly can be demonstrated by multidirectional tomography and high resolution CT (Fig. 7).

Enlargement of the retropharyngeal lymph nodes may also be demonstrated by CT (Fig. 1). Palpable enlargement of pre-auricular and upper cervical nodes has occasionally been noted with carcinoma of the ear, but before the advent of CT there was no way of demonstrating the retropharyngeal lymph nodes which drain the anterior part of the middle ear and Eustachian tube region.

The other routes of spread are upwards through the tegmen tympani and backwards through the mastoid air cells, then through the thin plate of bone

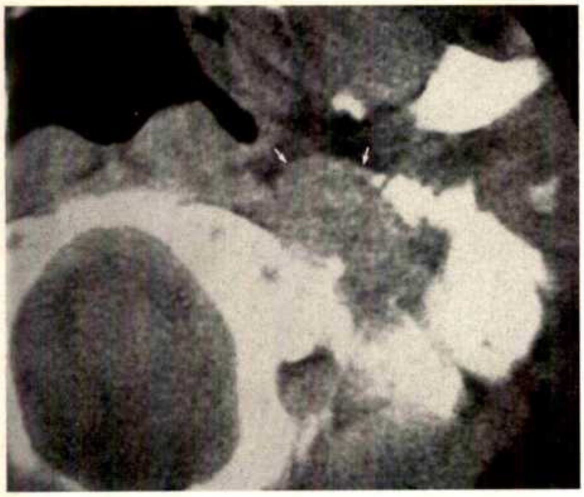


FIG. 7.

Axial CT scan showing extension of a middle ear carcinoma down the axis of the Eustachian tube. The growth has almost reached the styloid process and the fossa of Rosenmuller and is invading the deep lobe of parotid.

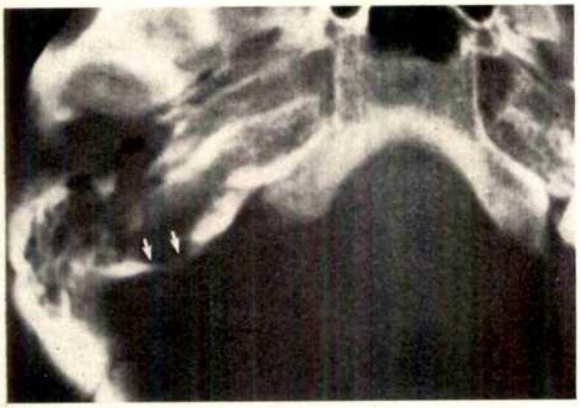


FIG. 8.

There is a soft tissue mass in the middle ear cavity which has eroded the back of the temporo-mandibular joint. The neoplasm has extended posteriorly through the mastoid air cells to erode the bony plate forming the back of the petrous pyramid (arrow).

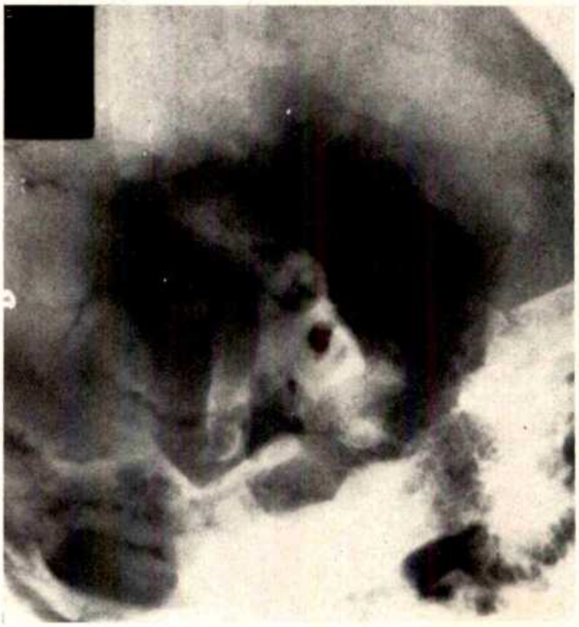


FIG. 9.

Extensive ragged erosion of the squamous temporal. A lateral oblique view showing the preservation of the labyrinthine capsule.

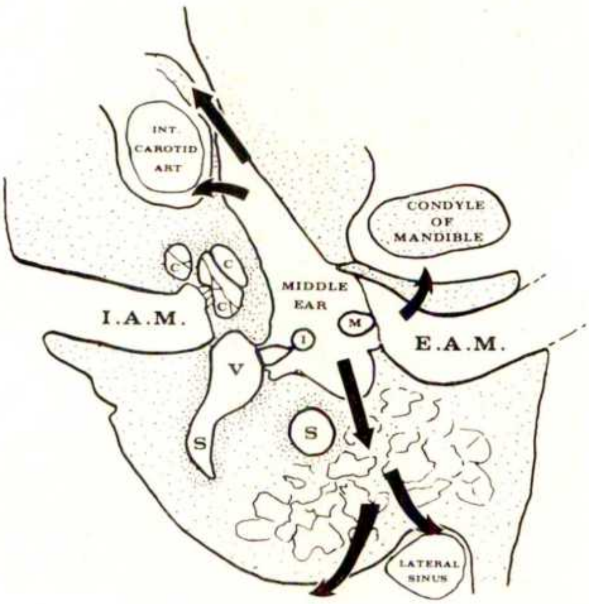


FIG. 10.

Diagram based on axial histological and tomographic sections of the petrous temporal bone. The arrows indicate the usual directions of spread of carcinoma of the middle ear and bony external auditory meatus. C = cochlea, V = vestibule, S = semicircular canal, I = incus, M = malleus. The top of the diagram is anterior.

forming the posterior wall of the pyramid and underlying the lateral sinus. Erosion of these thin bony structures may also be demonstrated radiologically (Fig. 8). Once inside the cranial cavity infiltration along the dura occurs, and when this is breached death soon follows. Therefore it seems unlikely that any significant extension into middle or posterior cranial fossae would be shown on a conventional CT brain scan. Similarly we can see no point in doing a carotid angiogram except to demonstrate a blocked lateral sinus. When the carotid artery itself is infiltrated then death soon follows. Nor can we agree that demonstration of cross-circulation is important (Clairmont and Conley, 1977) as we do not consider removal of the internal carotid a justifiable part of the procedure. Retrograde jugular venography however may be a useful investigation for assessing the extent of the disease by demonstrating obstruction of the lateral sinus by tumour.

Various regimes of treatment are used for carcinoma of the ear. Radiotherapy alone may be effective treatment for tumours of the external auditory meatus which do not involve the middle ear cleft (Lederman, 1965). For tumours of the middle ear radiotherapy is not satisfactory unless followed by some type of resection. Maran and Jacobson (1979) state "If the cancer is confined within the temporal bone and has not invaded the carotid canal then the choice of treatment is an *en bloc* temporal bone resection. Conversely if cancer lies outside the bony box then to remove that box is illogical." We believe that multidirectional tomography and especially high resolution CT enable a greatly improved estimate of tumour extension to be made, in spite of the infiltrative nature of squamous cell carcinoma of the ear.

CONCLUSIONS

1. Biopsy is essential for the early diagnosis of carcinoma of the ear, but radiology has two important subsidiary roles. Firstly, to suggest the likely diagnosis from the type of bone erosion, and secondly, to indicate the extent of the disease.

2. Petromastoid radiographs may show ragged bone destruction extending into the skull vault or floor of the middle cranial fossa, but these plain film appearances indicate advanced neoplastic disease. Erosion of the articular fossa of the temporomandibular joint is a common and important sign of carcinoma of the ear.

3. Multidirectional tomography in the lateral projection will best show erosion of the bony external auditory meatus. Roof, floor, anterior and posterior walls were all variously eroded in this series. Coronal section tomograms will demonstrate the extent of erosion of the middle ear cleft and skull base.

4. A common pathway of spread of carcinoma of the ear is by penetration of the thin bony septum separating the antero-medial aspect of the middle ear cavity from the intrapetrous portion of the carotid artery. Erosion of this septum can be demonstrated by coronal section tomograms, and is an important sign which may influence the treatment regime.

5. Penetration of the thin layer of bone between the posterior mastoid air cells and the dura is another important mode of spread of ear cancer. It is difficult to demonstrate radiologically but in one case was shown by high resolution axial CT.

6. High resolution CT gives good demonstration of bone erosion, especially of the anterior wall of external auditory meatus and middle ear. It is now the optimum method of demonstrating tumour spread in the axial plane, and frequently also in coronal section. Extension of the tumour as a soft tissue mass down the axis of the Eustachian tube into the infratemporal fossa, was well shown by high resolution CT.

7. Extension of tumour into the cranial cavity was not shown as a soft tissue mass in any of the cases. Intracranial extension is usually by a process of diffuse infiltration and rapidly kills the patient. Conventional brain scans therefore seem to have a limited role in the management of carcinoma of the ear. A venous jugulargram may be useful to show involvement of the lateral sinus.

REFERENCES

CHEN, K. T. K. and DEHNER, L. P., 1978. Primary tumours of the external and middle ear. *Archives of Otolaryngology*, *104*, 247–252.

CLAIRMONT, A. A. and CONLEY, J. J., 1977. Primary carcinoma of the mastoid bone. *Annals of Otology*, *86*, 306–309.

GOODMAN, M. L., 1971. Middle ear and mastoid neoplasms. *Annals of Otology*, *80*, 419–424.

KIM, B. H., 1971. Roentgenographic findings of malignant external otitis. *American Journal of Roentgenology*, *112*, 366–372.

LEDERMAN, M., 1965. Malignant tumours of the ear. *Journal of Laryngology and Otology*, *79*, 85–119.

LEWIS, J. S., 1960. Cancer of the ear. *The Laryngoscope*, *70*, 551–579.

LEWIS, J. S., 1973. Squamous carcinoma of the ear. *Archives of Otolaryngology*, *97*, 41–42.

LLOYD, G. A. S., PHELPS, P. D. and DU BOULAY, G. H., 1980. High resolution computerized tomography of the petrous bone. *British Journal of Radiology*, *53*, 631–641.

MARAN, A. D. G. and JACOBSON, I., 1979. Tumours of the ear. In *Clinical Otolaryngology*, (Blackwells, Oxford) p. 464–469.

MICHAELS, L. and WELLS, M., 1980. Squamous cell carcinoma of the middle ear. *Clinical Otolaryngology*, *5*, 235–248.

ZIZMOR, J. and NOYEK, A., 1969. Tumours and other osseous disorders of the temporal bone. *Seminars in Roentgenology*, *4* (2), 151–170.

1981, *British Journal of Radiology*, *54*, 110–116

Krypton 81m ventilation scanning in chronic obstructive airways disease

By D. A. Cunningham, B.M., B.Ch., M.R.C.P. and J. P. Lavender, F.R.C.P., F.R.C.R.

Department of Diagnostic Radiology, Hammersmith Hospital, Du Cane Road, London W12

(*Received April 1980 and in revised form October 1980*)

ABSTRACT

Ventilation and perfusion scans using $^{81}Kr^{m}$ and $^{99}Tc^{m}$-labelled macroaggregates have been studied in 60 patients with established chronic obstructive airways disease. Matched defects were found in all patients distributed throughout the lungs. Patients scanned during acute exacerbation frequently showed basal mismatched defects of ventilation (21 out of 30) and in a few follow-up scans showed resolution on treatment. Other patients also scanned in acute exacerbation showed unmatched defects of perfusion thought to represent pulmonary emboli. Poor correlation was found between scan defects assessed on a semi-quantitative basis and conventional lung function tests.

It has long been established that chronic obstructive airways disease gives rise to regional defects of ventilation and perfusion on radioisotope lung scans (Bentivoglio *et al.*, 1963; McKusick *et al.*, 1973; Secker-Walker and Siegel, 1973). The abnormalities are usually matched; while a basal distribution is observed in panacinar emphysema due to alpha 1 antitrypsin deficiency (Welch *et al.*, 1969), in patients with mixed bronchitis and emphysema there is a more even distribution of defects throughout the lungs (Alderson *et al.*, 1974a). Ventilation scans using ^{133}Xe have in fact been suggested as a sensitive method for detecting early chronic lung disease, as areas of decreased ventilation are frequently observed while the chest radiograph remains normal (Alderson *et al.*, 1974a).

Physiologically it has been shown that patients with established chronic lung disease have marked mismatching of ventilation and perfusion (Wagner *et al.*, 1977), but this is not usually apparent using conventional scanning techniques. This is in part due to the problems that arise when one compares the high-resolution image of regional perfusion obtained using technetium labelled particles, with the low-resolution images of regional ventilation obtained with xenon washout studies. To some extent this problem has been overcome by creating a "functional image" of regional ventilation to be compared with conventional perfusion images to give a ventilation/perfusion ratio (Secker-Walker *et al.*, 1972; Alderson *et al.*, 1974b). This method has been used to demonstrate a patchy distribution of ventilation/perfusion ratios in children with cystic fibrosis (Alderson *et al.*, 1974b). However, these so-called functional images of regional ventilation will never be truly comparable with technetium images of regional perfusion, owing to the markedly different energies of xenon and technetium which lead to differences both in resolution and in the volume of lung sampled.

$^{81}Kr^{m}$, a very short half-life cyclotron-produced gas, was introduced in 1975 (Fazio and Jones, 1975) as an alternative method of assessing regional ventilation. This gas produces high-resolution images which are directly comparable with those produced by technetium of regional perfusion. Patterns of ventilatory abnormalities and regional mismatching can therefore be assessed directly. We have used this method to study in detail 60 patients with established chronic obstructive airways disease (COAD).

MATERIALS AND METHODS

Patients

Sixty patients referred to the scanning unit were studied. All had definite evidence of COAD both on clinical grounds and on the basis of lung function tests. The majority of these patients showed a mixed pattern of emphysema and bronchitis. Approximately 10% showed features predominantly of emphysema (Burrows Type A) and a further 10% were predominantly bronchitic (Type B disease) (Burrows *et al.*, 1966).

Scanning techniques

$^{99}Tc^{m}$ labelled macroaggregates were used for regional perfusion and $^{81}Kr^{m}$ for ventilation. The technique used in obtaining ventilation scans using $^{81}Kr^{m}$ has been described elsewhere (Fazio and Jones 1975; Fazio *et al.*, 1978). This gas has such a short half-life that when inhaled continuously during normal tidal breathing it never equilibrates with alveolar gas and hence gives images which represent regional ventilation rather than lung volume. The images obtained are comparable with perfusion images using technetium-labelled macroaggregates.

Multiple images of ventilation and perfusion were obtained during tidal breathing using a large field of view gamma-camera (International G. E. Maxi) with a low-energy collimator. Line-spread functions for

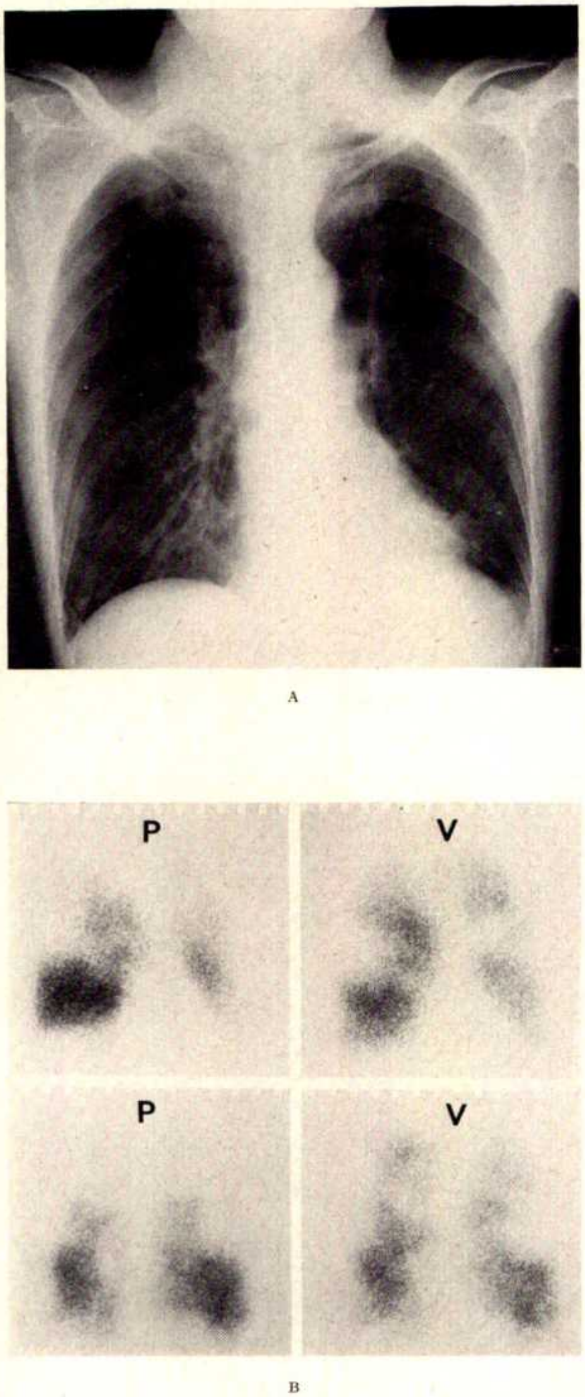


FIG. 1.

(A) Chest radiograph 13.4.76.

(B) Anterior (above) and posterior (below) perfusion and ventilation scans showing patchy matched defects in COAD 31.3.76.

The relative lack of apical perfusion is due to the fact that Tc macroaggregates are routinely injected with the patient erect.

^{99}Tc^{m} and ^{81}Kr^{m} with this collimator showed that similar resolution is obtained (FWHM for ^{99}Tc^{m} 6.25 mm; FWHM for ^{81}Kr^{m} 7 mm). The views taken included anterior, posterior and either lateral or posterior oblique views, and were identical for ^{81}Kr^{m} and ^{99}Tc^{m}. The contribution of counts from ^{99}Tc^{m} (140 keV) to the images of ventilation with ^{81}Kr^{m} (190 keV) represent approximately 5% of the total counts collected (300 k).

Assessment of scans and chest radiographs

Scan abnormalities were assessed subjectively, with reference to the pattern of abnormality and the regional distribution of ventilation and perfusion. Where mismatching was present or gross defects involving whole lobes or one lung were seen, chest radiographs were assessed blind by an independent observer.

Ventilation scans of those patients who had had formal lung-function tests within weeks of the scan were assessed using a semi-quantitative method described by Fazio *et al.* (1978). Using both anterior and posterior scans, each lung was divided into upper and lower zones and each zone was then scored subjectively by comparison with a normal scan on a scale from 0 to 4, where 0 = no activity and 4 = normal activity. The resulting scores from each zone were then added and correlated with FEV1, residual volume (RV) and total lung capacity (TLC) using Spearman's ranked correlation coefficient.

RESULTS

Patterns of abnormalities and their distribution

(a) *Matched defects.* Most patients showed multiple non-segmental defects matched for ventilation and perfusion (Fig. 1A, B) which were distributed evenly throughout the lungs. Scans from patients who were clinically purely emphysematous were compared with those who were clinically purely bronchitic but no convincing difference could be found between them.

Superimposed on these patchy defects were much larger abnormalities involving whole lobes or one lung. They occurred in about half our patients and involved upper, lower and middle lobe or lingula with equal frequency (Table I). With the exception of upper-lobe lesions which usually corresponded to radiographic evidence of apical fibrosis, presumably of tuberculous origin, radiographs failed to show abnormalities corresponding to the scan defects (Fig. 2A, B).

(b) *Mismatched defects.* Twenty-five patients showed areas of ventilation/perfusion mismatching.

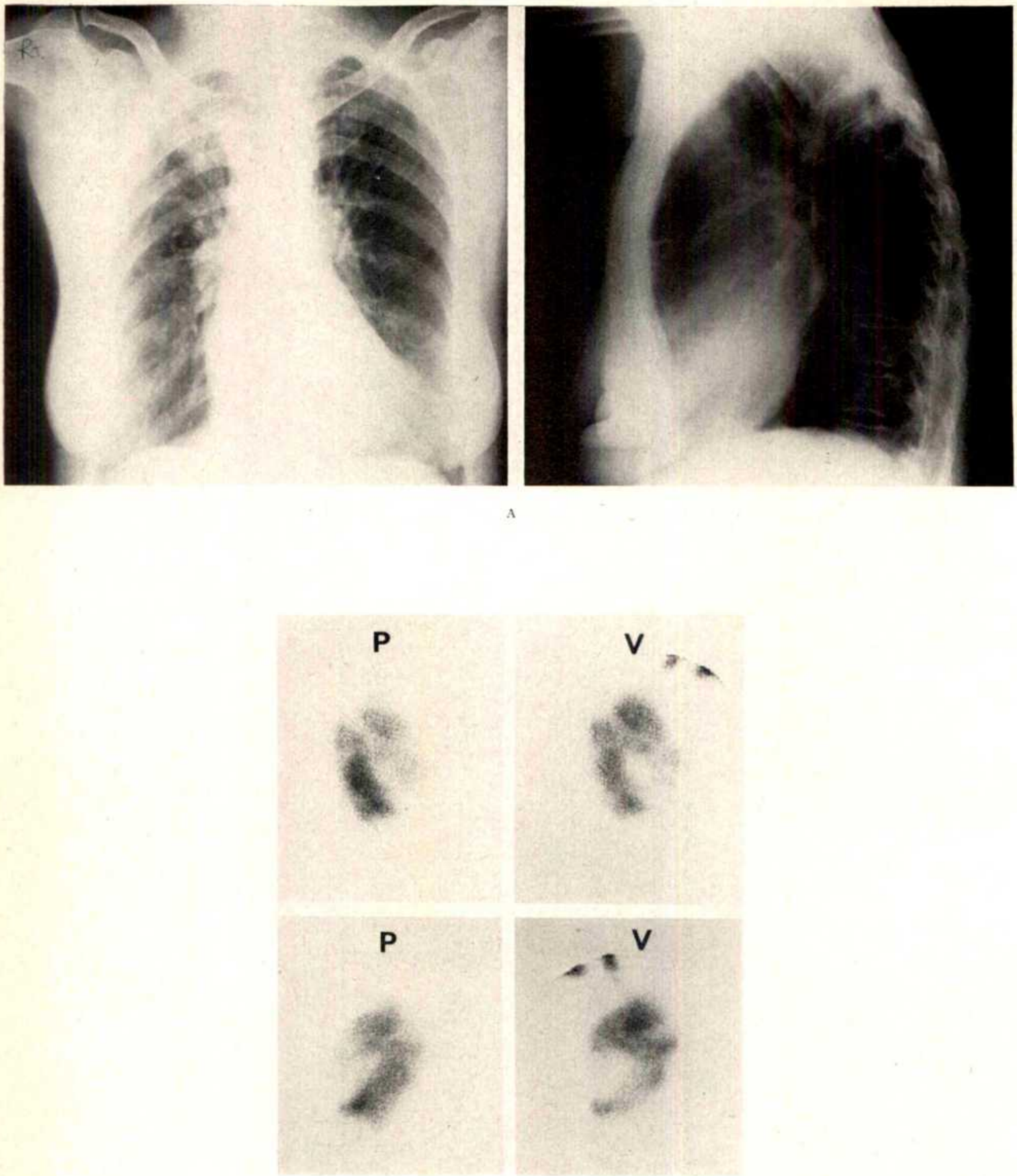


FIG. 2.

(A) Chest radiograph 31.12.78.

(B) Right (above) and left (below) lateral perfusion and ventilation scans showing large matched defects involving middle lobe and lingula 6.12.78.

TABLE I

DISTRIBUTION OF SCAN DEFECTS IN 29 PATIENTS WITH COAD WITH PREDOMINATELY LOBAR OR UNILATERAL DEFECTS

Distribution	No.	Chest radiographs examined	Radiographic findings	
Upper lobe	8 (6)*	7	Apical fibrosis Normal	5 2
Middle lobe/ lingula	7 (1)	4	Bronchiectasis Normal	1 3
Lower lobe	6 (5)	5	Normal	5
Whole lung	7	7	Bullae Normal	2 5

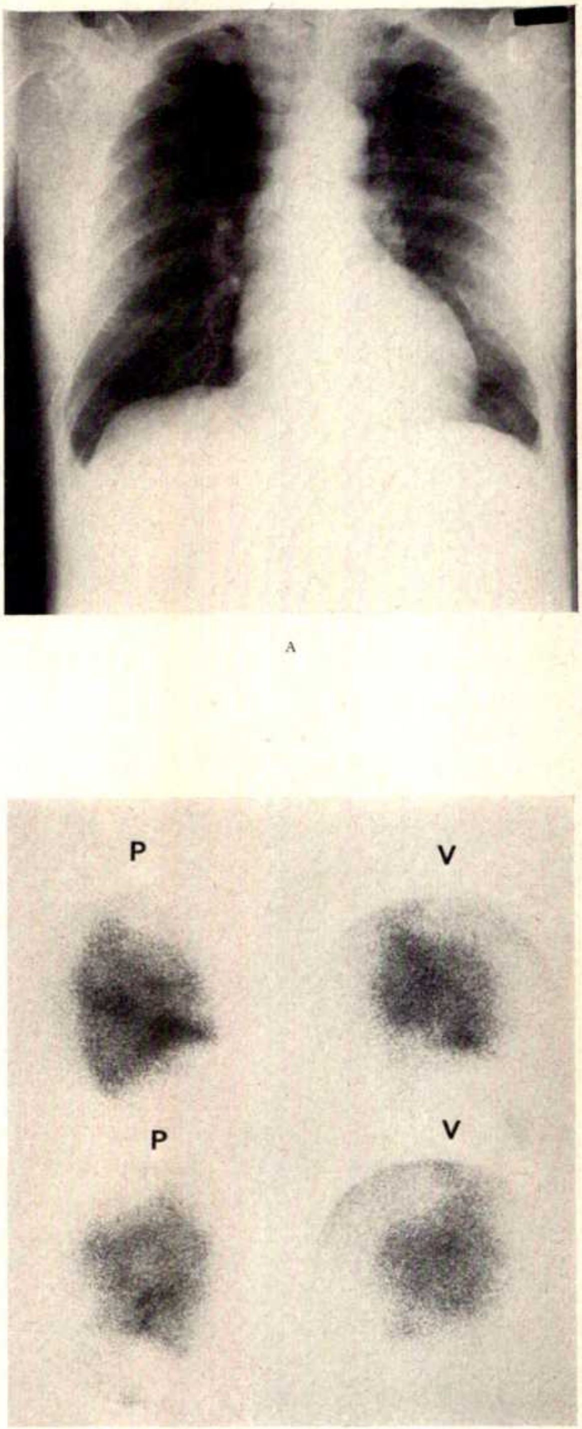
*( ) indicates patients in whom lesions were bilateral.

All of these were in-patients at the time of scanning, 21 having been admitted with acute exacerbation of COAD.

The most frequent abnormality was of unmatched defects of ventilation which occurred in 21 patients and was usually basal and bilateral. No corresponding radiographic abnormality was seen (Fig. 3A, B). Five patients showed unmatched defects of perfusion (one had mismatching in both directions). Two had been referred with a possible clinical diagnosis of pulmonary embolic disease, while a further three were in-patients with acute infective episodes. Defects of perfusion in these patients were felt to represent unsuspected pulmonary emboli. In one the source of emboli was found to be an asymptomatic right femoral vein thrombosis (Fig. 4A, B, C).

Follow-up scans

Fourteen patients had one or more follow-up scans at intervals between eight days and 23 months with a mean of seven months. Seven patients had matched defects only and no change was seen over the follow-up period. The remaining seven patients had mismatched defects at the time of the first scan. In six in whom the first scan was performed during an acute exacerbation, basal unmatched defects of ventilation were seen to resolve (Fig. 5A, B). Two of these patients in addition showed resolution of large matched defects. In neither case was there any radiographic abnormality corresponding to these defects. Two patients had unmatched defects of perfusion (one had mismatching in both directions). These were felt to represent pulmonary emboli and partial resolution occurred over six weeks and five months respectively.



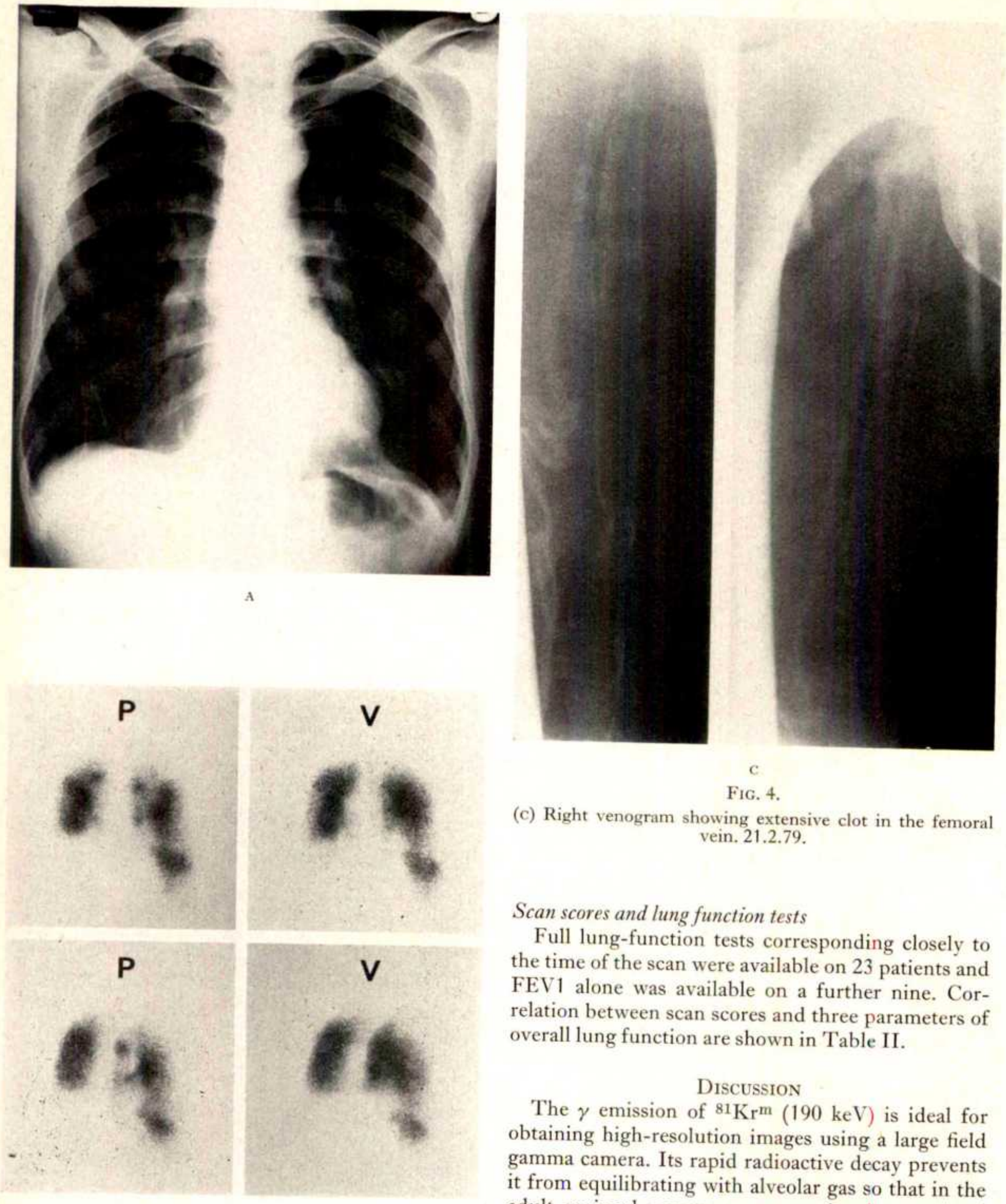
A

B

FIG. 3.

(A) Chest radiograph. 31.1.78.

(B) Right (above) and left (below) lateral perfusion and ventilation scans showing basal unmatched defects of ventilation during an acute exacerbation of COAD 30.1.78.



A

B

C

FIG. 4.

(A) Chest radiograph. 20.2.79.

(B) Posterior (above) and posterior oblique (below) perfusion and ventilation scans showing an unmatched defect of perfusion in the right upper lobe. Scattered matched defects are also present. 21.2.79.

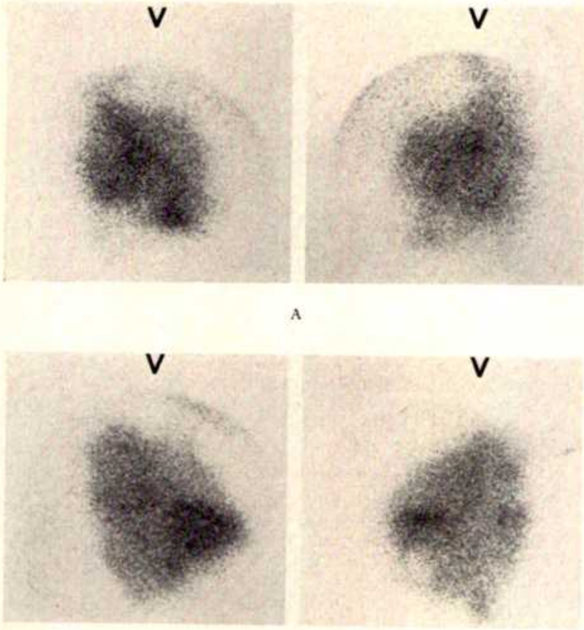
(C) Right venogram showing extensive clot in the femoral vein. 21.2.79.

Scan scores and lung function tests

Full lung-function tests corresponding closely to the time of the scan were available on 23 patients and FEV1 alone was available on a further nine. Correlation between scan scores and three parameters of overall lung function are shown in Table II.

DISCUSSION

The γ emission of $^{81}Kr^{m}$ (190 keV) is ideal for obtaining high-resolution images using a large field gamma camera. Its rapid radioactive decay prevents it from equilibrating with alveolar gas so that in the adult regional counts are proportional to regional ventilatory turnover. The relationship does not hold true when there is very high specific ventilation as in infants. In patients with COAD abnormalities of ventilation are due to areas where ventilatory turnover is reduced, and in this setting the images



A

B

FIG. 5.

Right and left lateral ventilation scans.

(A) 30.1.78 during an acute exacerbation.

(B) 6.2.78 following treatment. Resolution of basal ventilatory defects has occurred.

TABLE II

ANALYSIS OF LUNG FUNCTION TESTS AND SCAN SCORES IN 32 PATIENTS WITH COAD

Scan score vs.	r	p
% predicted FEV1	0.59	<0.001
RV	-0.39	<0.05
% predicted TLC	-0.22	>0.1

obtained are thought to be a true reflection of regional ventilation.

The similar γ-ray energies of ^{99}Tc^{m} and ^{81}Kr^{m} (140 keV and 190 keV respectively) ensure that comparable volumes of lung are imaged. When much lower energies are emitted, as with ^{133}xe, this will not be so. With such similar energies "crossover" from one to the other might present a problem, but for the rapid decay of ^{81}Kr^{m} which has effectively disappeared by the time perfusion images are taken. Some 5% "crossover" does occur from ^{99}Tc^{m} to ^{81}Kr^{m} but this is not felt to be significant.

Matched defects of ventilation and perfusion occurred in all our patients. Although it has been claimed that bronchitic patients show a more segmental distribution of abnormality (Fazio *et al.*, 1978), which is certainly true of patients with reversible airways obstruction, we were unable to distinguish between types of COAD on the basis of scan abnormalities. The similarities between the scans of our patients, even when clinically at either end of the spectrum of COAD, may be due to the fact that most had fairly advanced disease and some emphysema may well have been present in all patients, although this was not necessarily evident on lung-function tests.

The even distribution of scan defects throughout the lungs is in agreement with other series (Secker-Walker and Siegel, 1973; Alderson *et al.*, 1974). While pure panacinar emphysema is found pathologically in the lower zones and anteriorly (Thurlbeck, 1973) and this distribution is reflected in lung scans of patients with alpha 1 antitrypsin deficiency (Welch *et al.*, 1969), most patients with severe COAD have mixed panacinar and centrizonal emphysema. The latter predominantly affects the upper zone, and it may be that this combination of types of emphysema accounts for our finding an even distribution of scan abnormality.

Follow-up scans failed to show the appearance of new matched defects. The maximum interval between scans was only 23 months which is relatively short in the natural history of the disease. Two patients did show resolution of large matched defects which were first seen during acute exacerbation. These defects may have been due partly to obstructing bronchial lesions causing an increase in pressure behind the obstruction and thus compromising the blood flow. Hypoxic vasoconstriction alone will not adequately account for the appearance, as marked defects of ventilation are frequently observed in acute exacerbation while perfusion is preserved, either wholly or in part.

Mismatched defects were only observed in patients during hospital admission, and the vast majority of these were scanned during admission for acute exacerbation of their disease. The most frequently observed pattern was of basal ventilatory defects, but we do not feel that this represents basal infection so much as the accumulation of secretions in this area as the result of bed rest. Two of our patients who showed this abnormality were in fact admitted with acute gastrointestinal bleeds, and there is no evidence that they had chest infections in addition.

As regards unmatched defects of perfusion, two patients had suspected pulmonary emboli and we felt that the scan confirmed this. A further three were in-patients with acute infective episodes, and there was no clinical suspicion of embolic disease. None of these patients had a pulmonary angiogram which might have confirmed the diagnosis, as they all had severe COAD in acute exacerbation and it was felt inadvisable. One did have a positive venogram however. Despite our lack of angiographic data we feel that the correlation between unmatched defects of perfusion on scans and angiographically proven emboli is so close that we are justified in diagnosing emboli in these patients. They represent approximately 10% of the patients scanned during acute exacerbation, who may therefore represent a high-risk group from the point of view of embolic disease.

Comparison of scan scores with conventional tests of lung function revealed significant but only moderate correlation with two of the parameters used (FEV1 and RV) and no correlation with the third parameter, TLC. This relatively poor correlation is not surprising, as the scan is recording regional abnormalities of lung function and conventional respiratory function tests are looking at overall performance. It has been claimed that ventilatory scans using ^{133}Xe are more sensitive than overall tests of lung function in the early detection of COAD (Welch *et al.*, 1969). We cannot comment on the sensitivity of scanning with ^{81}Kr^{m} relative to lung-function tests on the basis of the present study, as we intentionally took patients with established COAD who had abnormal lung function.

REFERENCES

Alderson, P. D., Secker-Walker, R. H. and Forrest, J. V. 1974a. The detection of obstructive pulmonary disease. *Radiology*, *112*, 643–648.

Alderson, P. D., Secker-Walker, R. H., Strominger, D. B., McAlister, W. H., Hill, R. L. and Markham, J., 1974b. Quantitative assessment of regional ventilation and perfusion in children with cystic fibrosis. *Radiology*, *111*, 151–155.

Bentivoglio, L. G., Beeral, F., Stewart, P. B., Bryan, A. C., Ball, W. C. and Bates, D. V., 1963. Studies of regional ventilation and perfusion in pulmonary emphysema using xenon 133. *American Review of Respiratory Diseases*, *88*, 315–329.

Burrows, B., Fletcher, C. M., Heard, B. E., Jones, N. L. and Wootliff, J. S., 1966. Emphysematous and bronchial types of chronic airways obstruction. *Lancet*, *i*, 830–835.

Fazio, F. and Jones, T., 1975. Assessment of regional ventilation by continuous inhalation of radioactive krypton-81m. *British Medical Journal*, *iii*, 673–676.

Fazio, F., Lavender, J. P. and Steiner, R. E., 1978. Krypton-81m ventilation and technetium-99m perfusion scans in chest disease. Comparison with standard radiographs. *American Journal of Roentgenology*, *130*, 421–428.

McKusick, K. A., Soin, J. S., Cooper, M. and Wagner, H. N., 1973. Measurement of regional lung function in the early detection of chronic obstructive lung disease (abstract). *Journal of Nuclear Medicine*, *14*, 427.

Secker-Walker, R. H., Hill, R. L. and Baker, J., 1972. The measurement of ventilation using a small on-line computer. *Proceedings of the 3rd conference on Computer Applications in Radiology, Supplement.*

Secker-Walker, R. H. and Siegel, E. A., 1973. The use of nuclear medicine in the diagnosis of lung disease. *Radiological Clinics of North America*, *11*, 215–241.

Thurlbeck, W. M., 1973. Chronic bronchitis and emphysema. *Medical Clinics of North America*, *11*, 651–668.

Wagner, P. D., Dantzker, D. R., Dueck, R., Clausen, L. J. and West, J. B., 1977. Ventilation perfusion inequality in chronic obstructive pulmonary disease. *Journal of Clinical Investigation*, *59*, 203–216.

Welch, M. H., Richardson, R. H., Whitcomb, W. H., Hammarsten, J. F. and Guenter, C. A., 1969. The lung scan in alpha 1 antitrypsin deficiency. *Journal of Nuclear Medicine*, *10*, 687–690.

Book review

The Radiology of Tuberculosis. Ed. Benjamin Felson. pp. viii+149, 1979 (Grune and Stratton, New York) $21.50.
ISBN 0-8089-1248-8

This is a multi-author, relatively short book of 13 chapters. The most part is devoted to intra-pulmonary tuberculosis covering clinical and laboratory aspects as well as the radiology. Chapters are included to cover other mycobacterial pulmonary disease and the appearances of tuberculous disease in the immuno-suppressed patient.

The remainder contains chapters on tuberculosis affecting the bones and joints, the gastro-intestinal tract, the genito-urinary tract, the larynx and the cranial and intra-cranial structures.

Throughout the book the clinical and pathological details are discussed to give a good understanding of the radiological changes described. The continually changing incidence of tuberculosis is emphasized in different populations and in relation to world travel. The dependance on previous films for identification of slow progress is stressed and the balance between immunity and organism virulence is well made. The results of treatment on the radiological findings are described.

Although the great variability of the disease in the chest is shown well, some may feel that other systems are not sufficiently detailed.

This is essential reading for all trainee radiologists and has general appeal for undergraduate and postgraduate medical libraries.

A. B. Ayers.

1981, *British Journal of Radiology*, *54*, 117–121 FEBRUARY 1981

A longitudinal study of the growth of the nasopharynx and its contents in normal children

By W. D. Jeans, F.R.C.R., D. C. J. Fernando, D.M.R.D., M.R.C.P., A. R. Maw, F.R.C.S. and
B. C. Leighton, M.D.S.

Departments of Radiodiagnosis and Otolaryngology, University of Bristol and Bristol Royal Infirmary, and
Department of Orthodontics, King's College Hospital Dental School, University of London

(*Received June 1980*)

ABSTRACT

The areas of the nasopharynx and its contents have been measured on the lateral cephalometric radiographs of 41 normal children who had been examined at yearly intervals for a minimum of 12 years between the ages of three and 19. The means and standard deviations of the areas of the nasopharynx, the soft tissues and the airway have been calculated for each year from three to 11 and for alternate years to age 19.

The size and shape of the soft tissues of individual children are shown to vary from year to year, and the anterior convexity changes to a concave shape with maturity. The soft tissues appear to grow more rapidly from three to five than does the nasopharynx, with a consequent decrease in size of the airway at this period. Subsequently the soft tissue area remains relatively constant whilst the nasopharynx increases in size so that the airway progressively enlarges. There is a significant difference between the sexes in nasopharyngeal area from 13 onwards ($p < 0.005$).

Knowledge of the natural history of the growth of the nasopharynx and its contents is necessary both to understand the pattern of development in normal children and to assess the importance of variations from the normal. Lateral radiographs provide a simple method of seeing the outline of the nasopharyngeal soft tissues in relation to the airway in life, and the two-dimensional image correlates well with the size estimated at posterior rhinoscopy (Linder-Aronson and Henrickson, 1973).

The range in size of normal adenoids at different ages has continued to be difficult to ascertain ever since it was first commented that an abundance of material would be needed for this purpose (Symington, 1910). Physiological variations in the size of the nasopharyngeal airway are known to occur during sleep (Groth, 1933), during crying (Weitz, 1946), and with the position of the mouth (Pruzansky, 1975) due to movement of the soft palate. These normal changes emphasize the need for a standard technique of radiography. Lateral cephalometry has the advantage of a fixed distance between the focal spot and the film, a standard patient position, a beam centred accurately at right angles to the area of interest and a degree of magnification that can be calculated.

A group of normal children having lateral cephalometric radiographs over a number of years has been reviewed to establish the normal development of the nasopharynx.

MATERIAL

Measurements were made on 414 lateral cephalometric radiographs of 19 boys and 22 girls taken at yearly intervals. These children are members of a group followed at King's College Dental Hospital over a period of 20 years as part of an orthodontic research project to assess normal development. They joined the project, with their parents' consent, on the sole criterion of being born in King's College Hospital, and none had any otorhinological or pulmonary abnormality.

The minimum period of observation on any child in the present study was 12 years and the maximum 16 years, between the age of three and 19. The mean number of radiographs for each child was 10.1 and there was a mean of 31.8 radiographs available in each of the 13 age groups selected—yearly from three to 11 inclusive, and at 13, 15, 17 and 19 years.

METHOD

Films were taken by a standard technique of lateral cephalometry throughout the study. The beam was centred to the external auditory meatus with the head in the true lateral position and the child breathing through the nose with a closed mouth. The average radiographic factors were 70 kV and 40 mAs. The tube to film distance was 151 cm (5 feet) and the calculated magnification of the mid-line structures varied between 1.067 and 1.092; this was disregarded in subsequent measurements.

The radiological limits of the nasopharynx (Fig. 1) were defined as being bounded posteriorly and superiorly by the bony contour of the nasopharynx; inferiorly by a horizontal line drawn parallel to and 2 cm below a line joining the anterior and posterior nasal spines and extended back to the cervical spine; and anteriorly by a line perpendicular to the horizontal line, joining the roof at the junction of the anterior margin of the pterygoid plate with the base

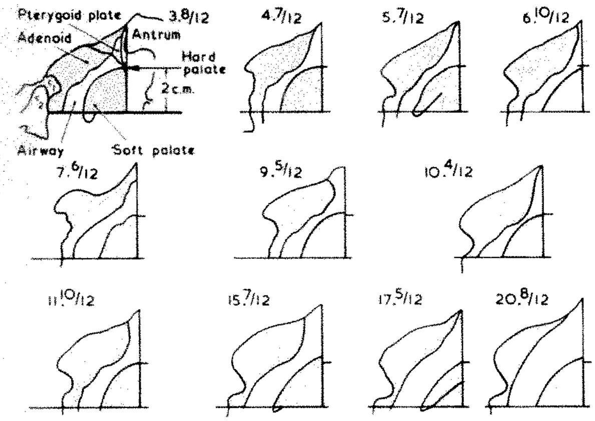


Fig. 1.

Variations in shape and size of the soft tissues and airway at different ages. Tracings from the lateral cephalometric films of the nasopharynx of one girl from age three to 20.

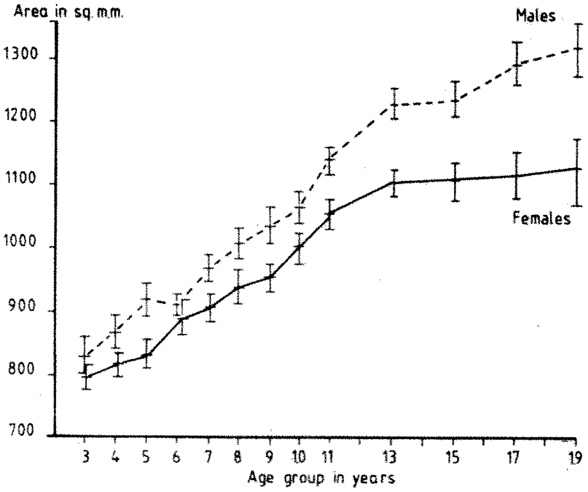


Fig. 2.

Mean area of the nasopharynx ± standard error. The change with age is shown in normal males and females.

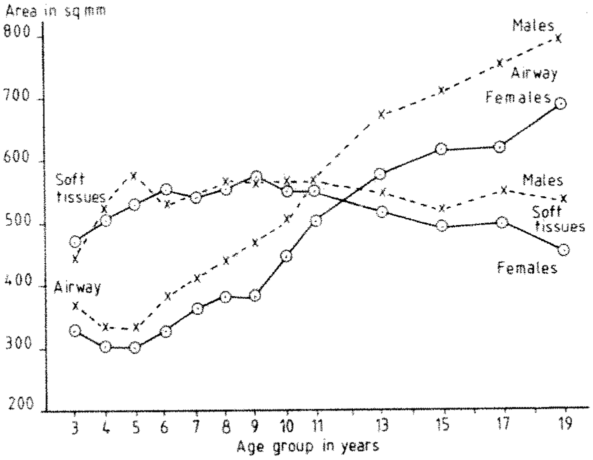


Fig. 3.

Mean areas of nasopharyngeal airway and soft tissues. The change with age is shown in normal males and females.

of the skull. The antero-inferior margin is formed by the soft palate.

Tracings of the nasopharyngeal margins and of the soft tissues and airway within it were made from the radiographs. The outlines of the soft tissues, the airway and the nasopharynx on the tracings were followed on a D-Mac tracing table linked to a PDP 8 computer which then printed out the areas within the outlines.

Results

The inter-observer agreement of the method was tested by asking two observers separately to trace and measure the areas concerned in 40 patients. The correlation coefficient for the two sets of measurements was 0.89. A total of 1230 measurements of the defined areas were made. Since there is no radiological distinction between adenoid, muscle or fascia they are referred to here collectively as the nasopharyngeal soft tissues.

Outline of nasopharyngeal soft tissues. Observations on consecutive tracings of individual children show that the outline of the soft tissues and the airway varies from year to year (Fig. 1). During development the inferior margin of the soft tissue outlined against the airway is convex and with maturity it becomes concave. The means and standard deviations of the areas of the nasopharynx, soft tissues and the airway were calculated (Table I).

The area of the nasopharynx increases from a mean of 827 mm^2 for boys and 799 mm^2 for girls at the age of three to 1324 mm^2 for boys and 1128 mm^2 for girls at age 19. The mean area for boys is slightly larger than that for girls up to age 11, and from 13 onwards is significantly larger ($p < 0.005$) (Fig. 2). The rate of increase accelerates from nine to 13 in girls and from ten to 13 in boys. It is much slower thereafter.

The area of the nasopharyngeal soft tissues increases from the age of three to five in boys; then, with minor fluctuations, remains the same until 19. In girls there is a steady increase from three until six followed by a gradual fall from 11 to the size present at 19 (Fig. 3). The difference in area between the sexes is significant at age five only ($p < 0.05$).

The area of the nasopharyngeal airway diminishes slightly from age three to five and then increases steadily up to age nine. There is a more rapid

TABLE I

MEANS AND STANDARD DEVIATIONS OF AREAS MEASURED IN SQUARE MILLIMETRES, FOR MALES AND FEMALES

	Age in years												
	3	4	5	6	7	8	9	10	11	13	15	17	19
Area in mm² Nasopharynx													
Males (1 SD)	827 (112.4)	864 (100.2)	920 (80.0)	909 (74.6)	969 (81.3)	1007 (104.2)	1036 (112.4)	1066 (95.8)	1140 (93.5)	1228 (82.5)	1234 (113.1)	1297 (145.1)	1324 (122.8)
Females (1 SD)	799 (87.5)	809 (61.6)	831† (99.5)	890 (83.1)	904 (96.4)	939 (118.1)	954 (97.3)	1001 (109.4)	1058 (118.4)	1101‖ (92.0)	1107‡ (131.6)	1116‖ (144.5)	1128‡ (174.3)
Soft tissues													
Males (1 SD)	448 (81.4)	526 (90.0)	581 (68.9)	531 (61.7)	545 (53.1)	567 (83.3)	564 (117.7)	564 (95.6)	567 (98.5)	554 (103.3)	521 (117.2)	549 (130.7)	536 (150.4)
Females (1 SD)	473 (84.0)	507 (39.3)	529* (56.3)	557 (72.1)	543 (87.3)	559 (76.2)	570 (88.1)	550 (82.3)	549 (79.1)	519 (87.9)	489 (89.5)	498 (86.5)	446 (112.8)
Airway													
Males (1 SD)	379 (93.3)	339 (98.9)	337 (86.0)	382 (62.9)	412 (61.5)	440 (77.8)	472 (130.2)	502 (121.9)	580 (98.8)	674 (88.8)	707 (91.3)	748 (110.3)	788 (102.3)
Females (1 SD)	326 (71.6)	302 (64.0)	302 (83.6)	333 (86.9)	362 (90.2)	384 (99.2)	385 (82.0)	447 (111.7)	509 (144.0)	580† (102.9)	618* (133.3)	618† (142.5)	681* (140.1)
Number of films													
Males	8	14	13	16	16	16	12	12	15	14	16	16	12
Females	15	11	20	20	19	19	16	19	18	18	19	19	15

Significant differences between males and females: $*p < 0.05$; $\dagger p < 0.01$; $\ddagger p < 0.005$; $\| p < 0.001$.

increase until 13, followed by a slower increase continuing up to 19. There is a significant difference ($p < 0.05$) between males and females from 13 onwards.

Discussion

The soft tissues in the nasopharynx are formed by the flexor muscles of the neck, the superior pharyngeal constrictor muscles, fascia, mucous membrane, and a quantity of lymphoid tissue that varies in amount at different ages. Linear measurement of the soft tissue thickness has shown that it is negligible for one month after birth, and then increases up to 24 months (Capitanio and Kirkpatrick, 1970). The thickness was found to be the same in girls and boys, and to stay almost constant from age two to 15 (Johannesson, 1968). The relationship of soft tissue width to nasopharyngeal airway has been used to produce a ratio showing that the airway is narrowest at age four (Fujioka *et al.*, 1979), and this has been confirmed in this study. The variations in shape of the nasopharyngeal tissues, illustrated in one child and seen in all the others followed during development, suggest that linear measurement of soft tissues at a fixed point may be an unreliable method of following changes in a group of children and we have preferred to measure the areas described. The inferior margin of the nasopharynx at the tip of the soft palate is variable in position. The fixed lower limit to the nasopharynx that we have used of 2 cm below the hard palate approximates to the level of the tip of the soft palate at all ages. Growth of the bony nasopharynx in the sagittal plane measured on lateral radiographs is mainly in height, the distance between the hard palate and the base of the skull increasing between 0.8 and 1.0 mm each year during growth, whilst the distance between the palate and the spine increases between 0 and 0.2 mm each year (Handelman and Osborne, 1976).

It has been shown that the size of adenoids in children coming to adenoidectomy was the same as those in a control group (Hibbert and Stell, 1979), and that symptoms caused by "enlarged adenoids" tend to occur in children having a relatively small nasopharynx (Linder-Aronson, 1970). Growth of the adenoids forms a major part of the enlargement of the nasopharyngeal soft tissues and produces the forward convexity seen on radiographs. This forward convexity is absent in children with agammaglobulinaemia in whom lymphoid tissue fails to develop normally (Margulis *et al.*, 1957). In adults it is abnormal to have a forward convexity (Eller *et al.*, 1971) and the serial tracings of individual children show the gradual change in shape from forward convexity to concavity with age. The finding in this study that the soft tissue area in boys is constant from six and that in girls falls slowly from nine to 19 suggests that there is a balance between the atrophy of the adenoid shown by its change in outline, and the increasing bulk of muscle which is greater in boys.

The differential rates of growth of neural, lymphoid, genital and general tissues have long been known (Scammon, 1930). It appears from this study that the nasopharyngeal lymphoid tissue grows more rapidly from three to five than does the nasopharynx, with a consequent reduction in size of the airway at this age. The subsequent increase in size of the nasopharyngeal area and the standstill in soft tissue size accounts for the progressive increase in airway from five onwards. The prepubertal spurt in growth rate of the nasopharynx starting at nine in girls and ten in boys leads to a significant difference in nasopharyngeal area between males and females from 13 onwards.

Acknowledgments

We are grateful to Mr. E. Turnbull for the illustrations, and to Mr. A. O. Hughes of the Department of Community Health, University of Bristol, for advice about the statistics.

REFERENCES

Capitanio, M. A. and Kirkpatrick, J. A., 1970. Nasopharyngeal lymphoid tissue. *Radiology*, *96*, 389–391.

Eller, J. L., Roberts, J. F. and Ziter, F. M. H., 1971. Normal nasopharyngeal soft tissue in adults. *American Journal of Roentgenology*, *112*, 537–541.

Fujioka, M., Young, L. W. and Girdany, B. R., 1979. Radiographic evaluation of adenoidal size in children: adenoidal-nasopharyngeal ratio. *American Journal of Roentgenology*, *133*, 401–404.

Groth, K. E., 1933. The roentgen picture of the epipharynx of children under normal conditions and by adenoid vegetations. *Acta Radiologica* (Stockholm), *14*, 463–469.

Handelman, C. S. and Osborne, G., 1976. Growth of the nasopharynx and adenoid development from one to eighteen years. *Angle Orthodontist*, *46*, 243–259.

Hibbert, J. and Stell, P. M., 1979. A radiological study of the adenoid in normal children. *Clinical Otorhinolaryngology*, *4*, 321–327.

Johannesson, S., 1968. Roentgenologic investigation of the nasopharyngeal tonsil in children of different ages. *Acta Radiologica* (Diagnosis) (Stockholm), 7, 299–304.

Linder-Aronson, S., 1970. Adenoids. Their effect on mode of breathing and nasal airflow and their relationship to characteristics of the facial skeleton and dentition. *Acta Oto-laryngology* (Stockholm), Suppl. 265.

Linder-Aronson, S. and Henrickson, C. O., 1973. Radiocephalometric analysis of anteroposterior nasopharyngeal dimensions in 6 to 12 year old mouth breathers compared with nose breathers. *Journal of Otorhinolaryngology (ORL)*, *35*, 19–29.

Margulis, A. R., Feinberg, S. B., Lester, R. G. and Good, R. A., 1957. Roentgen manifestations of congenital agammaglobulinaemia. *Radiology*, *69*, 354–359.

Pruzansky, S., 1975. Roentgencephalometric studies of tonsils and adenoids in normal and pathologic states. *Annals of Otology, Rhinology and Laryngology*, *84*, Suppl. 19, 55–62.

SCAMMON, R. E., 1930. The measurement of the body in childhood. In: Harris, J. A., Jackson, C. M., Paterson, D. G., and Scammon, R. E. *The Measurement of Man.* Minneapolis, University of Minnesota Press, pp. 173–215.

SYMINGTON, J., 1910. The Pharyngeal Tonsil. *British Medical Journal*, *2*, 1147–1148.

WEITZ, H. L., 1946. Roentgenography of the adenoids. *Radiology*, *47*, 66–70.

Book reviews

Cerebral Aneurysms: Advances in Diagnosis and Therapy. Edited by H. W. Pia, C. Langmaid and J. Zierski, pp. 468, figs. 143, tables xiv, 1979 (Springer-Verlag, Berlin/Heidelberg) DM198, $108.90

This is a beautifully illustrated and comprehensive monograph on cerebral aneurysms, based on the contributions of international experts to a workshop which took place in 1977. It is the first publication which adequately covers the advances in treatment which have taken place over the last few years and which have resulted in a greatly improved prognosis after subarachnoid haemorrhage. Only a few of the presentations are specifically radiological. The contributions on cerebral angiography emphasize the now well accepted advantages of using magnification and tomography and also describe the uses of intra-operative angiography. There are adequate discussions of the value of computed tomography in diagnosis and management. The technique and results of introducing detachable balloons for the treatment of carotid-cavernous fistulae and the indications for such balloons in arterial aneurysms are discussed by Debrun and Djindian in relation to their large personal experience.

There are other sections of some radiological interest dealing with morphology and aetiology of aneurysms and contributions on pathophysiology of spasm, blood flow and hydrocephalus following haemorrhage. Inevitably much of the book is devoted to treatment and surgical technique for aneurysms in particular situations, but even these parts contain some discussion of radiology among much useful background knowledge. This is a book which neuroradiologists will wish to peruse and use for reference.

B. E. KENDALL.

Advances in Neurosurgery. 7. Neurovascular Surgery. Specialized Neurosurgical Techniques. Ed. by F. Marguth *et al.* 1980 (Springer-Verlag, Berlin/Heidelberg/New York). DM.88.00 ISBN 0-387-09675-2

This volume contains papers based on the contribution to a joint meeting of North American and European, mainly German, neurosurgeons which took place in Munich in October 1978. The meeting was especially concerned with intracranial vascular surgery, techniques of operative approach, experimental surgery and chemotherapy, but there are a few contributions which are of particular interest to radiologists. These include:

1. An assessment by Sprung and Grume of the tests at present in use for predicting the results of shunting in normal pressure hydrocephalus. They emphasized the necessity for standardization of metrizamide CT and show that it is not reliable if used alone to predict response to surgical shunting.
2. Examination of circulation and metabolism of the brain by positron emission tomography by Yamamoto *et al.*, which describes the basic principles and applications of the method.
3. Applications of selective angiography by Wappenschmidt and Lins, and the treatment of intramedullary angiomas by H. W. Pia. Both these articles present the personal experience of experts using techniques which, in this rapidly advancing field, are now virtually routine.

There are other papers of academic interest, including identification of epileptic foci by contrast enhanced CT, and the recognition of minute cerebral gliomas, but relatively little of the book can be considered essential reading for radiologists and most of this has been published elsewhere.

B. E. KENDALL.

Correlative Sectional Anatomy of the Head and Neck. A Colour Atlas. By J. R. Thompson and A. N. Hasso. pp. xi+445. 1980. (YB Medical Publishers, London), £120·00. ISBN 0-8016-4934-X

Techniques which produce sectional images such as conventional, computed transmission and emission tomography and diagnostic ultrasound have a widespread and increasing application in diagnosis; nucleo-magnetic resonance may also be used to produce similar images. The importance of a detailed knowledge of *in vivo* cross sectional anatomy is therefore apparent. The usual anatomical section of organs, which have been removed from the body and fixed, lack many of the anatomical relationships which are important in *in vivo* diagnosis.

The authors, both neuroradiologists, have used a technique, which was developed for detailed correlation of polytomography of the temporal bone with anatomical sections, to produce exquisitely detailed large sections of the head and neck in the sagittal and coronal planes. Good, precisely comparable images made with a Philips polytome and EMI 5005 body scanner of the same specimen are included so that the images can be easily correlated. Post-mortem artefacts and the effects of freezing on the CT sections do not interfere with this correlation.

In addition to coronal and sagittal sections, the orbit and the ear are also shown in axial and oblique planes.

The book is beautifully produced and there is a good index. The only criticism is the lack of sections in the transverse axial plane; perhaps it was considered that this had been dealt with adequately in other publications. It is strongly recommended as a reference book to any radiologist dealing with sectional images of the head and neck.

B. KENDALL.

1981, *British Journal of Radiology*, *54*, 122–125

Recognition of the superscan in prostatic bone scintigraphy

By A. R. Constable, M.Sc., M.Inst.P. and *R. W. Cranage, M.A., D.Phil.

Department of Medical Physics, St. Paul's Hospital, Endell Street, London WC2

(*Received July 1980 and in revised form September 1980*)

ABSTRACT

Widespread bone metastases can occasionally give rise to a uniform distribution of ^{99}Tc^{m} methylene diphosphonate resulting in a superficially normal appearance on the bone scan. The scans are recognizable by the high ratio of bone to soft tissue activity, the absence of focal lesions in the axial skeleton, and there are usually no renal images. These "superscans" can occasionally be misinterpreted as normal. An index of image quantitation related to the ratio of bone to soft tissue uptake is shown to be capable of clearly distinguishing these patients from patients in other categories. The condition is thought to be more frequently associated with prostatic carcinoma than with other aetiologies.

Bone scintigraphy is now well established as the primary means of investigating patients with suspected bone metastases (Citrin *et al.*, 1977; McNeil, 1978) and it is now common for skeletal radiography to accompany scintigraphy only in cases where interpretation of the scan is equivocal.

Bone scintigraphy has an important role in the early detection of bone metastases in patients with prostatic carcinoma (O'Donoghue *et al.*, 1978) and serial scans can aid the clinician in the assessment of treatment response in these patients (Fitzpatrick *et al.*, 1978). Both of these studies have reported the incidence of prostatic carcinoma patients whose radiographs show widespread metastases and whose scans show a uniformly heavy uptake of labelled pharmaceutical. Such scans are similar in appearance to normal scans except for a greater contrast between bone and soft tissue and an absence or considerable reduction of activity in the kidneys. Similar scans have been previously reported (Sy *et al.*, 1975) and were referred to as "super bone scans" by Osmond *et al.* (1975).

Recognizing the super bone scan or "superscan" solely from the absence of renal images is clearly unsatisfactory. False negative superscans can arise in the presence of obstructive uropathy, a not uncommon finding in prostatic carcinoma patients and poor renal function can give rise to false positive superscans. In the absence of other recognition criteria it is all too easy to miss the superscan when bone scintigraphy is unaccompanied by routine skeletal radiography. The present study utilizes a simple index of image quantitation related to the bone uptake of radiopharmaceutical which clearly separates superscan patients from patients in other categories.

PATIENTS AND METHODS

All of the patients in our study were men between 40 and 80 years of age who had surgically proven prostatic carcinoma. All patients were given an intravenous injection of 370 MBq (10 mCi) of ^{99}Tc^{m} labelled methylene diphosphonate (MDP)† and gamma camera views of the axial skeleton were taken between 2½ and 3½ hours later using the Siemens/Searle LFOV camera linked to a Medical Data Systems PAD computer system (the MDS A^{2} system was used towards the end of the study). Posterior views of the lumbar and lower thoracic spine were stored on disc for later analysis.

In order to derive a quantitative index from a scan, regions of interest were placed over the 12th thoracic vertebra and over an area between the pelvic crest and the kidney (Fig. 1). The counts per unit area for the two regions were then used to calculate our "T12 index" – the ratio of the image intensity at T12 to that of soft tissue. No correction factors were used and no routine calculations were made to determine the absolute values of bone and soft tissue uptake nor to determine the actual uptake ratio.

The T12 region was selected for this purpose solely because of its central position in the axial skeleton and its ease of identification when more than one observer is involved. The exact placing of both areas was not found to be critical and reproducible determinations of the T12 index were made by different observers.

RESULTS

Twenty patients had normal bone scans with no evidence of metastatic disease at the time of the study. Figure 1 shows one of these patients with the regions used for quantitation superimposed on the scan. The T12 index for this group of patients covered the range 2.7 to 7.8 with a mean of 4.7±1.4 (SD).

Ten patients with focal lesions had T12 indices ranging from 2.4 to 6.8 with a mean of 4.8±1.5

---

*Present address: Medical Physics Dept., Musgrove Park Hospital, Taunton.

†Supplied by The Radiochemical Centre, Amersham.

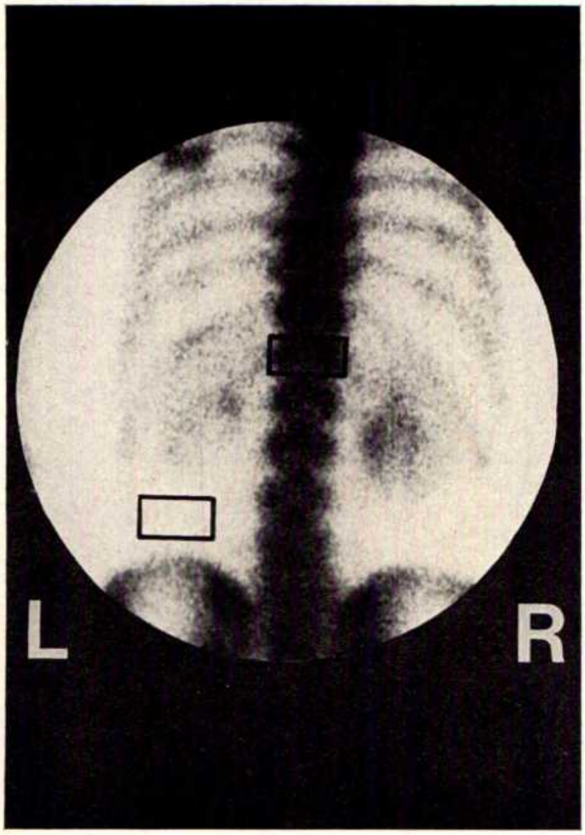


FIG. 1.

A normal bone scan. The two rectangles show the regions selected for determining the T12 index. One region is placed over the 12th thoracic vertebra and the other is placed above the pelvic crest and below the kidney.

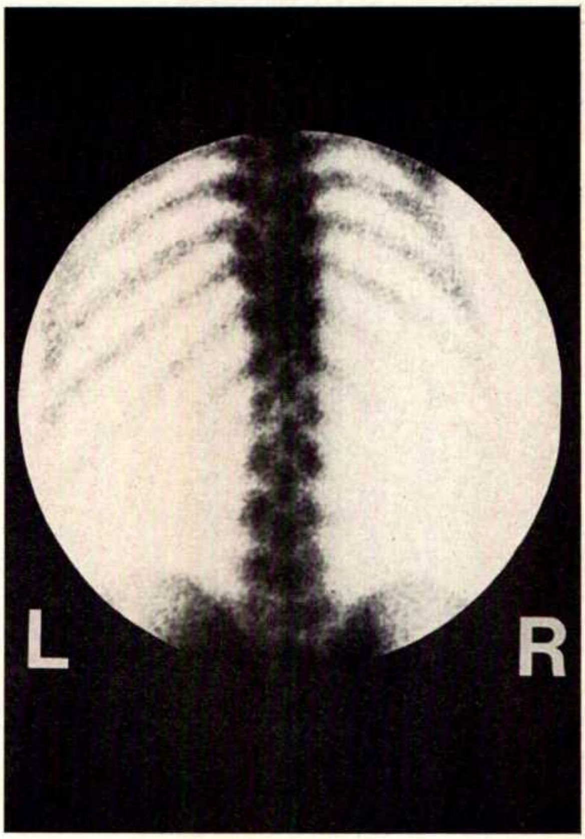


FIG. 2.

A typical "superscan" in which a heavy concentration of activity appears in all bones, a low concentration appears in background tissue and a characteristic absence of renal images appears.

(SD). No patient in this group had a focal lesion at T12 but an additional patient with extensive discrete metastases and not included in this study had an "L2 index" of 5.4 on one occasion and 5.5 a month later.

Four patients with superscans confirmed radiologically to have widespread bone metastases had T12 indices ranging from 17 to 24.2 with a mean of 20.2 ± 3.6 (SD). Figure 2 shows one of these superscan patients with the typical absence of renal images. Figure 3 shows another superscan patient in which one renal image is present due to a right-sided obstruction.

The above results are summarized in Fig. 4 and show the clear separation between superscan and normal patients ($p \ll 0.0001$). It is interesting to note that there is no significant difference in the T12 index between normal patients and those with focal lesions.

Fourteen patients with discrete spinal metastases had ratios of lesion to soft tissue ranging from 5.1 to 16.8 with a mean of 8.3 ± 3.5 (SD) and one patient on haemodialysis with no appreciable kidney function had a T12 index of 9.9.

DISCUSSION

Our results show that superscan patients can be clearly distinguished from patients in other categories by using a simple T12 index of image quantitation.

The spread of values in normal patients and patients with focal lesions reflects the range of renal function as well as the range of bone to soft tissue mass. In patients with normal renal function, about 60% of the ^{99}Tc^{m} MDP is excreted in the urine during the first three hours after injection (Subramanian *et al.*, 1975). In patients with reduced renal function more of the radiopharmaceutical is available for bone uptake leading to a higher T12 index in these patients. Our one dialysis patient with a T12

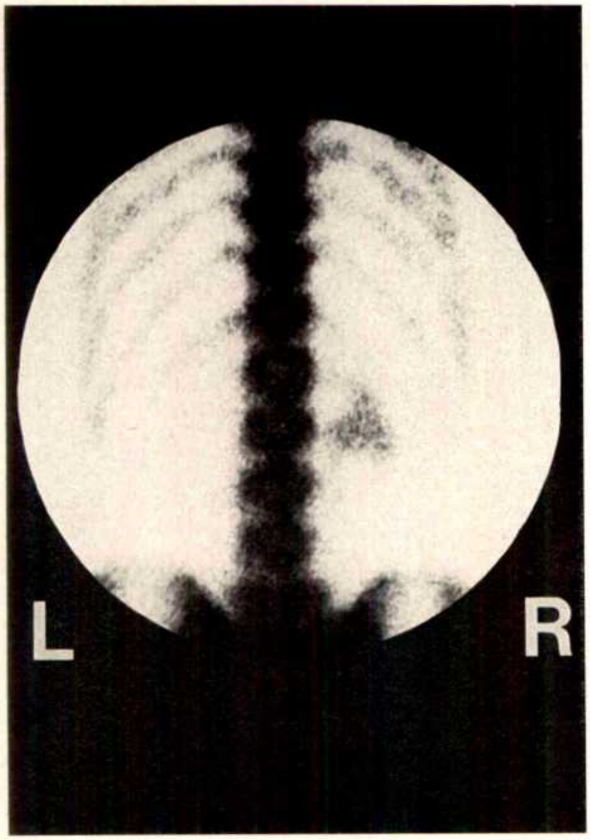


FIG. 3.

This patient has widespread prostatic metastases and the T12 index of 17 enables the scan to be defined as a "superscan" despite the appearance of a renal image. The patient had a right renal obstruction.

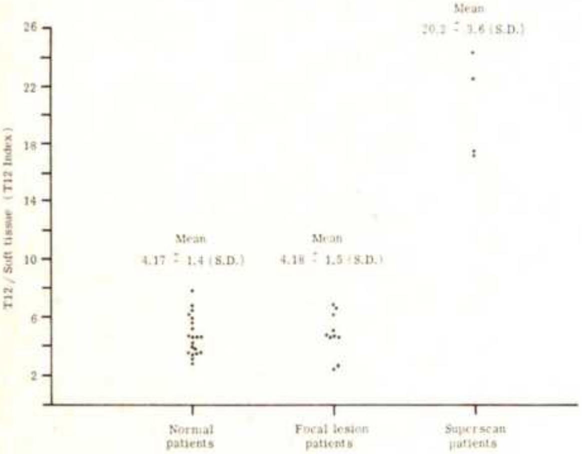


FIG. 4.

The T12 index for "superscan" patients is seen to be significantly different from the values obtained for both normal patients and those with focal metastases.

index of 9.9 provides some indication of a limiting value arising from poor renal function.

Superscan patients have an avidity of uptake of ^{99}Tc^{m} MDP in bone which is far in excess of normal patients or patients with widespread discrete metastases. In two of our superscan patients it was possible to measure the amount of activity excreted in the urine in the first three hours after injection. This was found to be 9% in one patient and 13% in the other; five to six times less than normal patients. Bone uptake in these patients is very rapid and our measurements suggest that 85% of the injected dose goes to bone compared with less than 40% in normal cases. Although our T12 index for superscan patients has a mean value of 20.2, the few measurements we have been able to carry out on these patients suggests the actual bone to soft tissue uptake ratio is in the region of 80 compared with a figure of about 16 for normal patients and patients with focal lesions; again a factor of about five.

It is not the intention of the present study to offer explanations for the extraordinarily high bone uptake in superscan patients. Nor can we say with complete assurance whether the superscan denotes progression of disease when it follows a condition of discrete metastases, though this appears usually to be the case.

The superscan condition appears to be more frequently associated with prostatic cancer than with other aetiologies. Osmond *et al.* (1975) used ^{99}Tc^{m} diphosphonate in 259 patients including 91 with prostatic cancer and reported the superscan appearance in prostatic patients only. Of the seven superscan patients reported by Sy *et al.* (1975), six had prostatic cancer and one had cancer of the bladder. Three probable superscan cases were reported by Thrupkaew *et al.* (1974) using ^{18}F and ^{99}Tc^{m} diphosphonate. Two of these patients had breast carcinoma and the other had prostatic carcinoma. Frankel *et al.* (1974) reported a patient with an apparently normal scan but whose radiographs showed widespread sclerotic and lytic lesions. This 25-year-old patient was diagnosed as having histiocytic lymphoma and the scan appearances were thought to be due to lymphoma involvement in every bone. The scans were performed with ^{99}Tc^{m} polyphosphate and there was a uniform heavy uptake throughout the axial skeleton but there were clear renal images making it a questionable superscan.

Citrin *et al.* (1977), in a large series including 283 breast and 14 prostatic carcinoma patients, used various ^{99}Tc^{m} phosphate compounds and did not include the superscan as a finding despite having reported it as a possible interpretation problem in earlier work (Citrin, 1977).

As an indication of the incidence of the superscan condition in patients with prostatic cancer, we have retrospectively reviewed 539 patients, all of whom had X-ray skeletal surveys as well as bone scintigraphy. 136 had positive scans, 22 of which were diagnosed as superscans (18 of them without the aid of the T12 index). If these results are typical, about 17% of patients with prostatic metastases can be expected to have superscans either at presentation or during follow-up. This high prevalence suggests the need for unequivocal recognition criteria in routine bone scintigraphy. Our own index of image quantitation provides a simple, reliable means of identifying the superscan and should eliminate the possibility of incorrect or equivocal interpretation.

REFERENCES

CITRIN, D. L., 1977. Problems and limitations of bone scanning with ^{99}Tc^{m}-phosphates. *Clinical Radiology, 28,* 97–105.

CITRIN, D. L., BESSENT, R. G. and GRIEG, W. R., 1977. A comparison of the sensitivity and accuracy of the ^{99}Tc^{m}-phosphate bone scan and skeletal radiograph in the diagnosis of bone metastases. *Clinical Radiology, 28,* 107–117.

FRANKEL, R. S., JOHNSON, K. W., MABRY, J. J. and JOHNSON, G. S., 1974. "Normal" bone radionuclide image with diffuse skeletal lymphoma. *Radiology, 111,* 365–366.

FITZPATRICK, J. M., CONSTABLE, A. R., SHERWOOD, T., STEVENSON, J. J., CHISHOLM, G. D. and O'DONOGHUE, E. P. N., 1978. The assessment of treatment response in carcinoma of the prostate. *British Journal of Urology, 50,* 555–561.

MCNEIL, B. J., 1978. Rationale for the use of bone scans in selected metastatic and primary bone tumours. *Seminars in Nuclear Medicine, 8,* 336–345.

O'DONOGHUE, E. P. N., CONSTABLE, A. R., SHERWOOD, T., STEVENSON, J. J. and CHISHOLM, G. D., 1978. Bone scanning and plasma phosphatases in carcinoma of the prostate. *British Journal of Urology, 50,* 172–177.

OSMOND, J. D., PENDERGRASS, H. P. and POTSAID, M. S., 1975. Accuracy of ^{99}Tc^{m}-diphosphonate bone scans and roentgenograms in the detection of prostate, breast and lung carcinoma metastases. *American Journal of Roentgenology, 125,* 972–977.

SY, W. M., PATEL, D. and FAUNCE, H., 1975. Significance of absent or faint kidney sign on bone scan. *Journal of Nuclear Medicine, 16,* 454–456.

SUBRAMANIAN, G., MCAFEE, J. G., BLAIR, R. J., KALLFELZ, F. A. and THOMAS, F. D., 1975. ^{99}Tc^{m} Methylene diphosphonate—a superior agent for skeletal imaging: comparison with other technetium complexes. *Journal of Nuclear Medicine, 16,* 744–755.

THRUPKAEW, A. K., HENKIN, R. E. and QUINN, J. L., 1974. False negative bone scans in disseminated metastatic disease. *Radiology, 113,* 383–386.

Book review

Atlas of Computerized Emission Tomography. By P. J. Ell, J. M. Deacon and P. H. Jarritt, pp. 225, 1980 (Churchill-Livingstone, London), £45·00.
ISBN 0-443-022283

This is the first atlas devoted to radioisotope emission tomography. It covers the clinical experience of this technique based on the use of the Cleon tomographic brain and body imagers on 208 patients. Sadly these devices are no longer commercially available. However, the pictures are similar to those produced by any single photon emission device and the experience gained on this device can be applied equally to other commercial systems.

The book commences with an introductory chapter on the basic principles of emission tomography, comparing and contrasting the different approaches to this technique and reviewing briefly the various clinical applications, especially in relation to other types of imaging.

The next 172 pages start with presentations of the normal brain anatomy seen on cross section. With each set of illustrations is a brief clinical history and the interpretation of the brain scintigram, CET scan and CT scan if included. Vascular and neoplastic lesions are described as well as secondary lesions involving the skull. This section helps to illustrate *in vivo* the physical performance of the system confirming that the focal areas of increased activity actually lie within the skull bone on cross section!

The latter part of the clinical section contains case histories and illustrations of the use of single-photon emission tomography (SPET) in the lung, liver, spleen and heart. While the illustrations of the brain are obvious and easy to follow, those involving these organs are more difficult.

The clinical sections conclude with a review of the clinical material with a detailed discussion of the methods and results. In general the results of CT and CET are comparable. Overall one is left with the impression that CET is a distinct and valuable step forward in diagnostic imaging.

The last sections in the book deal with specific information on the Cleon 710 and 711 imagers. Although these are no longer made the sections are interesting as they show how performance characteristics and calibration can be achieved. The book ends with a fairly comprehensive bibliography of papers on emission tomography.

This is an extremely useful book both to show "non-users" the potential and value of emission tomography and for those who are using SPET devices. Its value is in the excellent reproduction of the images which are full size rather than the usual miniscule pictures seen in scientific papers. The authors are to be congratulated on producing this book at just the right time.

V. R. MCCREADY.

1981, *British Journal of Radiology*, 54, 126–131

Mediastinal lymphoscintigraphy in ovarian cancer using intraperitoneal autologous technetium-99m-labelled erythrocytes

By W. D. Kaplan, M.D., W. D. Bloomer, M.D., A. G. Jones, Ph.D., J. Federschneider, M.D. and R. C. Knapp, M.D.

Departments of Radiology, Radiation Therapy, and Obstetrics and Gynecology, Harvard Medical School; Joint Program in Nuclear Medicine, Joint Center for Radiation Therapy, and Brigham and Women's Hospital, Boston, Massachusetts, USA

(*Received May 1980 and in revised form September 1980*)

ABSTRACT

$^{99}Tc^{m}$-labelled autologous erythrocytes (approximately 2.0 ml and 2.0 mCi) were administered intraperitoneally (IP) to 15 patients with ovarian cancer. Anterior abdominal images were then collected for up to six hours to evaluate both the dynamics of intraperitoneal tracer distribution and the potential for visualizing internal mammary lymph nodes as correlated with the presence of diaphragmatic tumour. Results indicated that dispersion of red cells closely resembled that seen during IP contrast studies; the distribution patterns were heterogeneous, remained constant with time, and were intimately related to bowel peristalsis. Visualization of internal mammary lymph nodes indicated patency of diaphragmatic lymphatics; non-visualized nodes correlated with the presence of diaphragmatic tumour. The test had a sensitivity of 0.80 and a specificity of 0.90 for defining disease. Results of this study suggest use of $^{99}Tc^{m}$-red blood cells as a diagnostic test for diaphragmatic involvement by ovarian cancer and as a method for monitoring the effects of therapy.

Ovarian cancer continues to be the leading cause of death from gynaecological malignancies. Its natural history is characterized by two major routes of dissemination (Feldman *et al.*, 1972; Knapp and Friedman, 1974). The more common route is direct seeding of tumour cells from the ovary into the peritoneal cavity. These tumour cells can then metastasize to the upper abdomen, omentum, and diaphragmatic surfaces. The other route is via lymphatic channels to retroperitoneal lymph nodes.

Much effort has recently been directed to identifying those patients who have early dissemination. Laparoscopy has allowed visualization of diaphragmatic surfaces, confirmation of tumour spread in patients otherwise unsuspected of harbouring disease outside the pelvis, and objective evaluation of therapy in patients with advanced disease (Rosenoff *et al.*, 1975; Piver *et al.*, 1978).

A number of clinical and laboratory observations suggest that occlusion of diaphragmatic lymph channels by tumour cells leads to the development of ascites (Holm-Nielsen, 1953; Allen and Raybuck, 1960; Hirabayashi and Graham, 1970; Fastaia and Dumont, 1976; Bronskill *et al.*, 1977). In mice bearing intraperitoneal tumour cells, Feldman *et al.* (1972) found marked impairment in the egress of ^{51}Cr labelled erythrocytes from the peritoneal cavity prior to the development of ascites. Furthermore, this impaired drainage was correlated histologically with the presence of tumour cells obstructing the diaphragmatic lymphatics.

Because the lymphatics of the diaphragm drain into the mediastinum primarily via the internal mammary chain (Rouvière, 1932), these nodes are commonly visualized scintigraphically in patients following intraperitoneal injection of radiocolloid (Anghileri, 1968; Atkins *et al.*, 1970). A lack of visualization has been associated with the presence of overt ascites and may indeed be specific for malignant ascites (Coates *et al.*, 1973). Furthermore, mediastinal lymphoscintigraphy has been shown to be a sensitive indicator for small numbers of tumour cells in an experimental model and can be used to predict the cell kinetics of developing malignant ascites (Bloomer and Adelstein, 1979).

Based upon these observations, we speculated that intraperitoneally administered autologous $^{99}Tc^{m}$-labelled erythrocytes could be used in patients with ovarian cancer for imaging mediastinal activity and thus provide a diagnostic tool for assessing diaphragmatic involvement by tumour. Because of the more unfavourable characteristics of ^{51}Cr, $^{99}Tc^{m}$ was selected as the erythrocyte radiolabel for use in this study.

MATERIALS AND METHODS

Autologous erythrocytes were labelled with $^{99}Tc^{m}$ using the technique described by Smith and Richards (1976). A 6 ml sample of peripheral whole blood

---

This work was supported in part by a grant CA–12662 from the National Cancer Institute, DHEW, a grant GM 23270 from the US Public Health Service, and a contract EY–76–S–4115 from the Department of Energy.

Address correspondence and reprints requests to: William D. Kaplan, M.D., Division of Nuclear Medicine, Sidney Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, USA.

was drawn up into a sterile vacutainer tube containing 2.0 μg tin, 3.67 mg sodium citrate, and 5.5 mg dextrose. The blood was incubated at room temperature for five minutes; 4 ml of sterile saline was then added and incubation continued for an additional five minutes. The tube was then centrifuged at 1500 rpm for five minutes in an inverted position to sediment the erythrocytes against the stoppered end. Labelling was performed by withdrawing 2–3 ml of packed erythrocytes into a syringe containing 75–150 MBq (2–4 mCi) of ^{99}Tc^{m} as pertechnetate in 1.0 ml of normal saline.

Between January 1977 and September 1979, 28 patients with ovarian cancer were considered for investigation; 13 were excluded because their tumours were of borderline malignancy, because intra-abdominal adhesions precluded adequate intraperitoneal dispersion of labelled erythrocytes, or because erythrocyte labelling efficiency was less than 90%. Thus 15 patients were available for analysis. The diaphragmatic surfaces of all patients were examined for the presence of tumour either at laparotomy or by peritoneoscopy within four weeks of lymphoscintigraphy. Informed consent was obtained from each patient studied. An indwelling catheter was placed within the peritoneal cavity through a lower quadrant puncture. Catheter placement was documented by radiographs of the abdomen following the instillation of iodinated contrast material.

Scintiphotos were obtained on Searle scintillation cameras using either diverging collimation with an instrument with a small field of view or parallel-hole low-energy all-purpose collimation for an instrument with a large field of view. With patients positioned supine under the camera, 2 ml of the autologous ^{99}Tc^{m}-labelled erythrocyte suspension was introduced into the abdomen. The catheter was then gently flushed with 20 ml normal saline. Sequential 500 000 count anterior abdominal and pelvic scintiphotos were obtained after injection. Scintiphotos were accumulated at approximately five-minute intervals for the first 30 minutes; images were then obtained every 15 minutes over the next hour. Patients were then allowed to ambulate, returning for additional images of the pelvis, abdomen and thorax at approximately two-hour intervals. Imaging was terminated when visualization of mediastinal lymph nodes occurred. If no intrathoracic nodes were visualized by five to six hours, patients were re-examined the following day. Selected images were stored on a Digital Equipment Corporation PDP/1140 computer in a 64×64 digital display for later analysis.

RESULTS

Sequential scintigraphic images of the abdomen showed initial accumulation of radioactivity within the pelvis at the site of the catheter tip. Dispersion progressed rapidly to the right paracolic gutter and subphrenic space with additional spread occurring along the left paracolic gutter (Fig. 1). Subsequently, radioactivity was noted along the caudad surface of the liver, inferior border of the stomach at the omental attachment, and at the root of the small mesentery (Fig. 2). Dispersion was usually complete within five to six hours and closely resembled that observed with iodinated contrast material (Fig. 3). The dispersion of radioactivity was heterogeneous

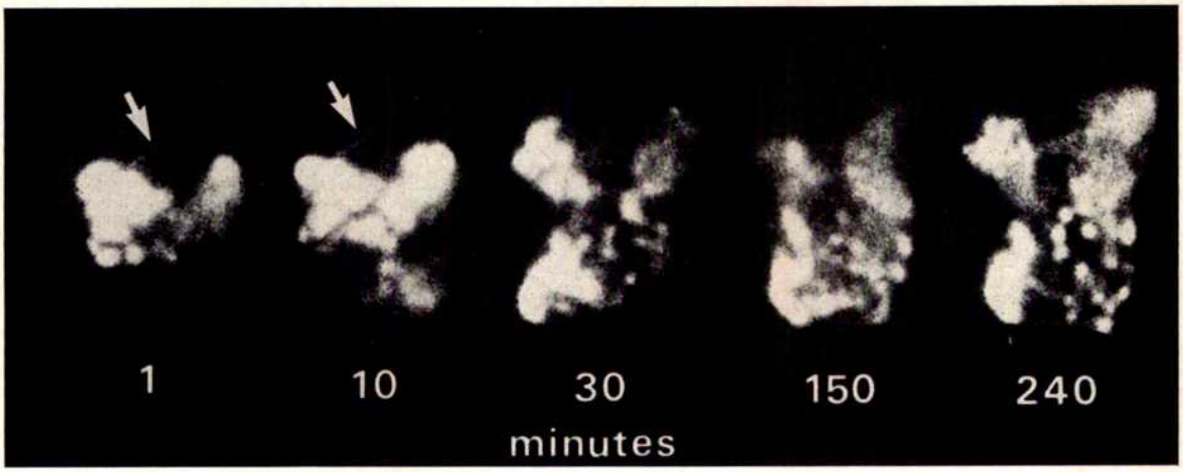


FIG. 1.

Sequential 500 000 count anterior abdominal images of intraperitoneal ^{99}Tc^{m}-labelled autologous erythrocytes over four hours. Arrow denotes catheter.

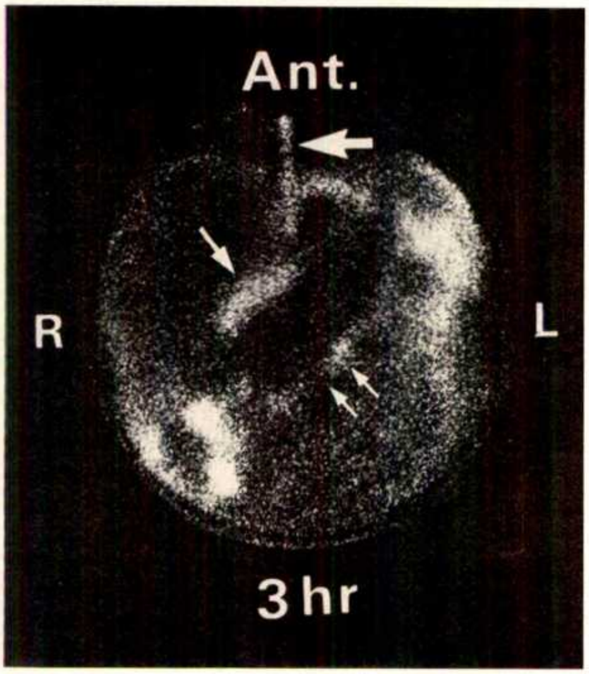


Fig. 2.

^{99}Tc^{m}-labelled autologous red cells at three hours migrating to the subphrenic, periportal (single small arrow) and subhepatic (double small arrows) spaces. Large solid arrow denotes linear cobalt strip overlying xyphoid.

and, once completed, showed little change in distribution even when patients were re-examined the following day (Fig. 4). Although visualization of mediastinal lymph nodes could be defined as early as 30 minutes after injection, activity in this region usually developed between two and five hours (Fig. 5). When visualized, the relative intensity of mediastinal nodes increased with time.

Five of 15 patients had confirmed diaphragmatic tumour involvement. Of these five, four had positive lymphoscintiscans (*i.e.* non-visualization of mediastinal lymph nodes), while the remaining one demonstrated visualization of mediastinal nodes. Ten patients had no involvement of the diaphragm. Nine demonstrated visualization of mediastinal lymph nodes, and one patient showed no visualization. The scintigraphic assessment of tumour involvement of the diaphragm using intraperitoneal labelled erythrocytes had a sensitivity of 0.80 and a specificity of 0.90 (McNeil *et al.*, 1975).

Discussion

Sequential scintigraphic imaging of the abdomen after the intraperitoneal injection of autologous ^{99}Tc^{m}-labelled erythrocytes has enabled us to follow the dispersion and distribution of radiolabelled material throughout the abdomen. The pathways of erythrocyte dispersion closely mimic those seen with iodinated contrast material (Fig. 3) (Myers, 1973).

The precise mechanism underlying dispersion of

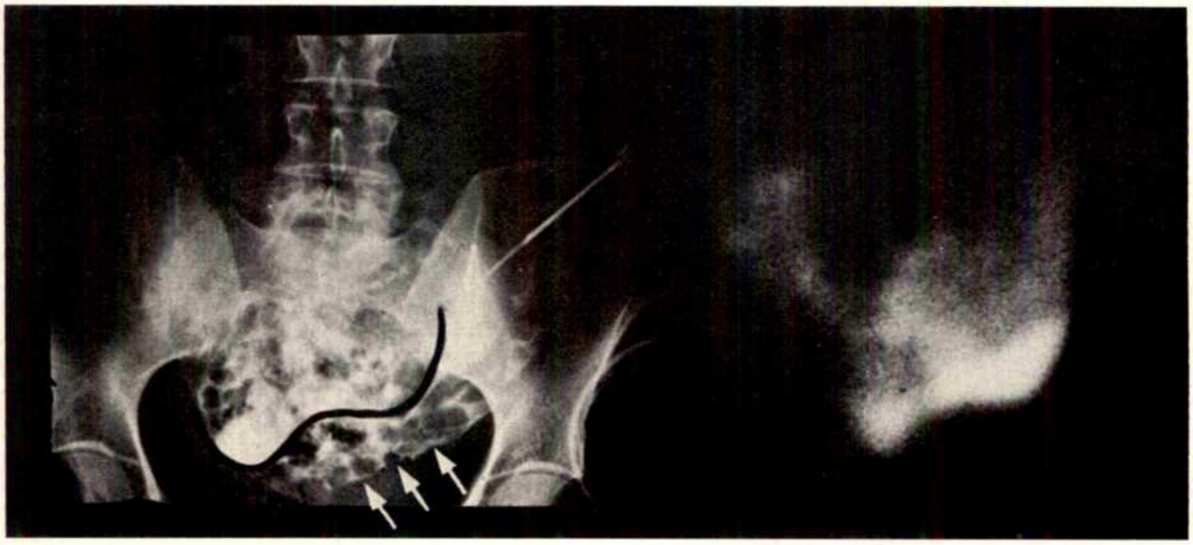


Fig. 3.

Views of the peritoneal cavity following contrast (left) and ^{99}Tc^{m}-red cells (right) in the same patient. Note similarity of distribution patterns (black line). Three arrows define most inferior distribution of contrast.

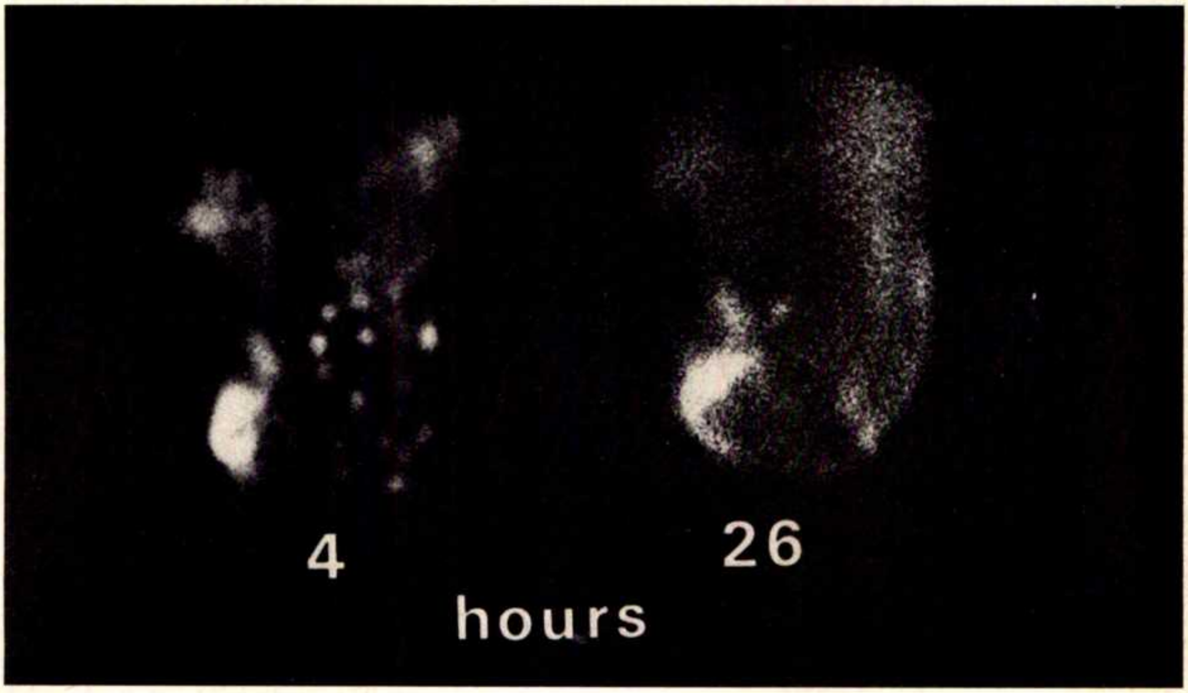


FIG. 4.
Anterior abdominal images of ^{99}Tc^{m}-erythrocytes in the same patient at four and 26 hours.

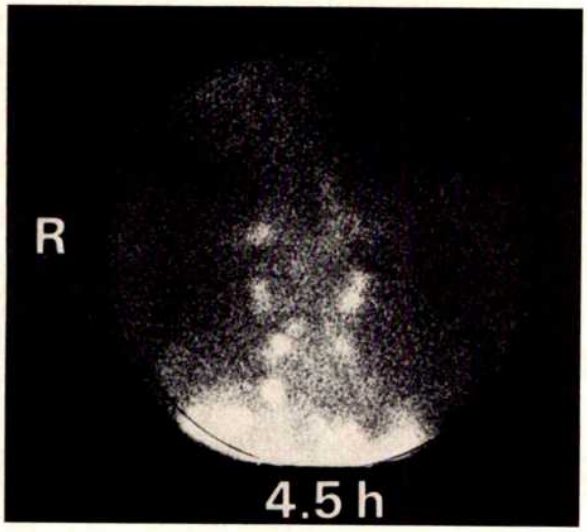


FIG. 5.
Anterior 500 000 count view of the thorax at 4.5 hours showing internal mammary lymph nodes bilaterally.

intraperitoneally injected substances remains a matter of conjecture. However, inasmuch as all patients in our series remained supine and essentially motionless during the initial 60 minutes after injection of labelled erythrocytes and the total volume administered was less than 25 ml, intestinal peristalsis is probably a major factor in abdominal dispersion. Indeed, final distribution of radioactivity did not appear to be influenced by gravity or heavy respiration.

Egress of radiocolloids from the peritoneal cavity has been demonstrated to proceed via the diaphragmatic lymphatics into the mediastinum with the internal mammary lymph nodes representing the primary route of drainage (Rouvière, 1932; Coates *et al.*, 1973). Routine lateral views in our patients confirm these reports (Fig. 6).

This study also confirms earlier observations on malignant ascites in an experimental tumour model using radiolabelled erythrocytes and colloid (Feldman *et al.*, 1972; Bloomer and Adelstein, 1979). We continue to believe that early spread of tumour to the diaphragm with involvement of lymphatic channels plays an important role in the development of malignant ascites. However, other and as yet undetermined mechanisms may also be involved at this early stage of dissemination. A recent study using ^{99}Tc^{m}-sulphur colloid in patients with ovarian tubal carcinoma reported a specificity similar to our experience but a much lower sensitivity (Katz *et al.*, 1979). The delay of two to five hours needed for ^{99}Tc^{m}-sulphur colloid definition of mediastinal

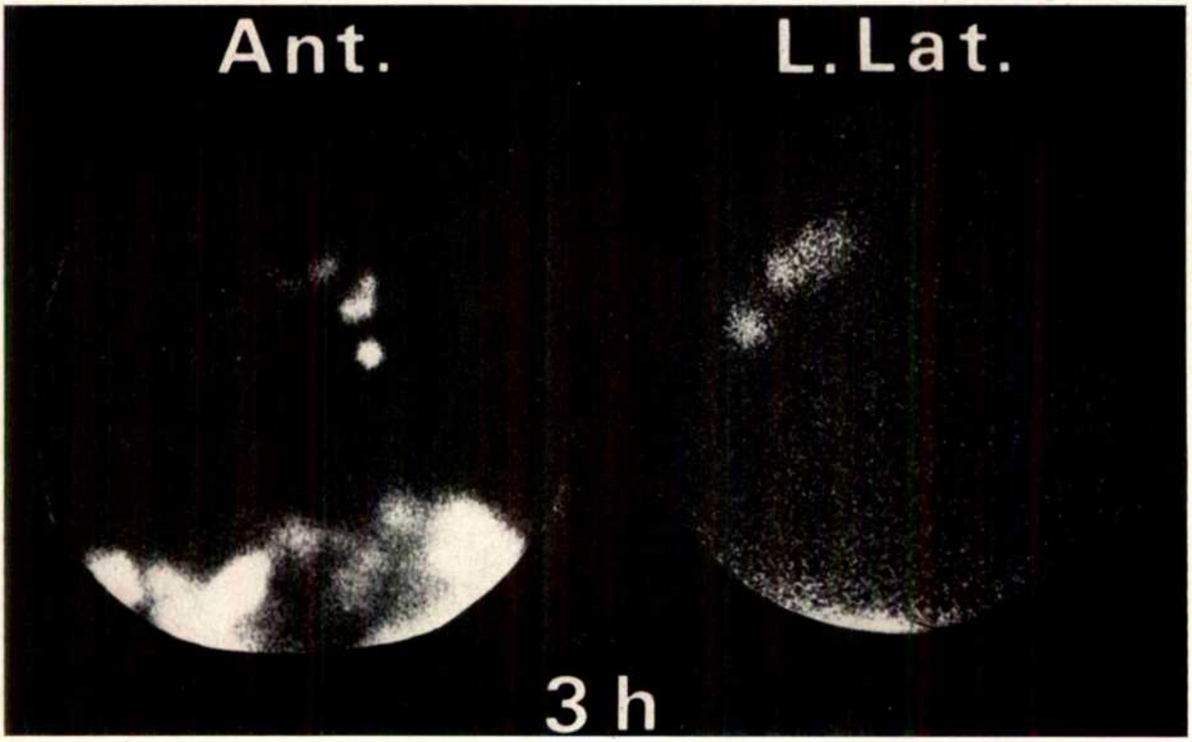


FIG. 6.

Anterior and left lateral scintiphotos of the thorax at three hours showing internal mammary lymph nodes.

lymph nodes could allow for intraperitoneal redistribution of tracer. With time, the amount of radiocolloid in the peritoneal fluid decreases relative to that trapped within the cellular fraction; thus, less tracer is available for transdiaphragmatic migration (Kaplan *et al.*, 1978).

From our data, it appears that ^{99}Tc^{m}-labelled autologous erythrocytes may offer a more sensitive agent for the scintigraphic definition of diaphragmatic tumour. Mediastinal lymphoscintigraphy by this technique may prove to have special significance in the clinical evaluation of patients with ovarian cancer not only as a diagnostic test for defining early peritoneal dissemination, but also as a noninvasive technique for monitoring responses to therapy.

ACKNOWLEDGMENTS

The authors thank Elaine N. Dufresne and Christopher Black for their technical assistance; John Buckley and Deborah Hansen for their photography and art work; and Barbara Connolly for her assistance in the preparation of the manuscript.

REFERENCES

ALLEN, L. and RAYBUCK, H. E., 1960. The effects of obliteration of the diaphragmatic lymphatic plexus on serous fluid. *Anatomical Record*, *137*, 25–32.

ANGHILERI, L. J., 1968. Uptake of colloidal chromic phosphate in the mediastinal lymph nodes. *Acta Radiologica: Therapy, Physics, Biology*, *7*, 202–208.

ATKINS, H. L., HAUSER, W. and RICHARDS, P., 1970. Visualization of mediastinal lymph nodes after intraperitoneal administration of ^{99m}Tc-sulfur colloid. *Nuklear Medizin* (Stuttgart), *9*, 275–278.

BLOOMER, W. D. and ADELSTEIN, S. J., 1979. Mediastinal lymphoscintigraphy reflects cell kinetics of developing malignant ascites. *British Journal of Radiology*, *52*, 756–758.

BRONSKILL, M. J., BUSH, R. S., and EGE, G. N., 1977. A quantitative measurement of peritoneal drainage in malignant ascites. *Cancer*, *40*, 2375–2380.

COATES, G., BUSH, R. S. and ASPIN, N., 1973. A study of ascites using lymphoscintigraphy with ^{99m}Tc-sulfur colloid. *Radiology*, *107*, 577–583.

FASTAIA, J. and DUMONT, A. E., 1976. Pathogenesis of ascites in mice with peritoneal carcinomatosis. *Journal of the National Cancer Institute*, *56*, 547–549.

FELDMAN, G. B., KNAPP, R. C., ORDER, S. E. and HELLMAN, S., 1972. The role of lymphatic obstruction in the formation of ascites in a murine ovarian carcinoma. *Cancer Research*, *32*, 1663–1666.

HIRABAYASHI, K. and GRAHAM, J., 1970. Genesis of ascites in ovarian cancer. *American Journal of Obstetrics and Gynecology*, *106*, 492–497.

HOLM-NIELSON, P., 1953. Pathogenesis of ascites in peritoneal carcinomatosis. *Acta Pathologica et Microbiologica Scandinavica*, *33*, 10–21.

KAPLAN, W. D., DAVIS, M. A., UREN, R. F., WISOTSKY, T., LATEGOLA, M., 1978. A model for the radionuclide measurement of ascitic fluid volumes. *Journal of Nuclear Medicine*, *19*, 1138–1141.

KATZ, R. D., ROSENSHEIN, N. B., ALDERSON, P. O., and

Wagner, H. N. Jr., 1979. Abdominal mediastinal lymphoscintigraphy in patients with ovarian carcinoma. *Journal of Nuclear Medicine*, *20*, 646.

Knapp, R. C. and Friedman, E. A., 1974. Aortic lymph node metastases in early ovarian cancer. *American Journal of Obstetrics and Gynecology*, *119*, 1013–1017.

McNeil, B. J., Keeler, E. and Adelstein, S. J., 1975. Primer on certain elements of medical decision making. *New England Journal of Medicine*, *293*, 211–215.

Myers, M. A., 1973. Peritoneography: Normal and pathologic anatomy. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine*, *117*, 353–365.

Piver, M. S., Barlow, J. J. and Lele, S. B., 1978. Incidence of subclinical metastases in stage I and II ovarian carcinoma. *Obstetrics and Gynecology*, *52*, 100–103.

Rosenoff, S. H., DeVita, V. T., Hubbard, S. and Young, R. C., 1975. Peritoneoscopy in the staging and follow-up of ovarian cancer. *Seminars in Oncology*, *2*, 223–228.

Rouviere, H., 1932. *Anatomic des Lymphatiques de l'Homme.* (Masson, Paris), pp. 160–165, 339–401.

Smith, T. D. and Richards, P., 1976. A simple kit for the preparation of ^{99m}Tc-labeled red blood cells. *Journal of Nuclear Medicine*, *17*, 126–132.

Book reviews

Handbuch der medizinischen Radiologie. Band XIII, Teil 2. Röntgendiagnostik des Urogenitalsystems: Weibliches Genitale (Encyclopaedia of Medical Radiology. Vol. XIII, Part 2. Roentgen Diagnosis of the Urogenital System: Female Genitals) Edited by C. Diethelm, F. Heuck, O. Olsson, F. Strnad, H. Vieten and A. Zuppinger. 474pp., 1980 (Springer–Verlag, Berlin/Heidelberg/New York), DM.360.

Although the title pages and preface are given in German and English this is not really a bilingual book as only one chapter is in fact written in English.

The book is comprehensive in extent. It commences with hysterosalpingography and then passes on to an interesting and unexpected section on paediatric gynaecology. Chapters on angiography and gynaecological tumours follow including one chapter in rather uneasy English on diagnostic help in radiotherapy planning. This leads on to further sections on the bladder and obstetrics including pelvimetry and ultrasound.

Each clinical section is self-contained so that all relevant methods *i.e.* plain films, contrast examinations, ultrasound and CT are included. This approach reflects a school of thought in this country which (rightly) believes that radiological specialization should be clinically rather than technically orientated.

Some detailed criticisms may be made. The section on urinary incontinence allots a very significant amount of space to the rather doubtful "wash-basin chain" method of cysto urethrography while no consideration is given to dynamic pressure-flow studies; further, there can hardly be any useful understanding of pelvimetry without relating the derived measurements to fetal presentation at delivery.

This book therefore shows that much is common in practice between here and Germany. The coverage is conventional and complete. The inclusion of CT examination for tumours and recurrence in the pelvis is welcome.

Although very commendable and excellently produced this volume probably has little to attract the English speaking radiologist.

J. H. H. Highman.

Radiation Oncology – Rationale, Technique, Results. By W. T. Moss, W. N. Brand and H. Battifora, 5th edit, pp.x+648, 1979 (YB Medical Publishers, Chicago/London), £29·95. ISBN 0-8016-3556-X

This is an excellent textbook of radiotherapy, for it succeeds in combining a humane philosophy of cancer care with a well informed rational basis for radiation therapy. The radiotherapy techniques which are described are conventional and safe.

The preface to this fifth edition begins "Recent knowledge has had a major impact on the contribution of radiation to the care of the cancer patient". Information on this major impact is not, however, evident in this book. For example, the important problem of the radioresistance of hypoxic tumour cells is discussed in detail but possible answers to this problem such as neutron therapy and the use of electron affinic radiosensitizers are not, and radiotherapy with hyperbaric oxygen is dismissed in a line as having "... for the most part been abandoned". New dose – time – volume relationships are also described; although the authors give good reasons for continuing to prefer equal, daily fractions for radical and often palliative treatment, they only hint that in the future fractionation may be tailored to cell kinetics. Electron therapy, now well established, gets scant attention and new afterloading techniques for interstitial and intracavity irradiation are not mentioned.

A chapter is devoted to the inter-relationship between radiotherapy and surgery and there are interesting sections on pre-operative radiotherapy and on irradiation of the intact breast after lumpectomy. The inter-relationship between radiotherapy and chemotherapy is, however, not well covered and the book lacks a chapter on this subject, needed even if only to show how one may modify or preclude the other and to put recent advances into perspective.

In spite of these criticisms, this represents one of the best textbooks of radiotherapy. It is well written and well illustrated and, as the authors intended, it is an excellent introduction to the art of the radiotherapist.

Thelma D. Bates.

1981, *British Journal of Radiology*, *54*, 132–135

Different fractionation schemes tested by histological examination of autopsy specimens from lung cancer patients*

By H. J. Eichhorn, Dr. med.

Zentralinstitut für Krebsforschung der Akademie der Wissenschaften der DDR, Bereich Experimentelle und Klinische Strahlentherapie, 1115 Berlin-Buch, Lindenberger Weg 80, GDR

(*Received March 1980 and in revised form October 1980*)

ABSTRACT

The biological effects of different fractionation schemes have been evaluated by the histological examination of bronchial carcinomas removed at operation or autopsy following radiotherapy. Radiation was given in daily, small fractions (200 cGy (rad)), large fractions (600 cGy (rad)) every fifth day, or a single high dose followed by daily low-dose treatment. The highest proportion of tumours free of viable cells was found in patients who had received small daily fractions in both operable and inoperable tumours. A hypothesis is put forward to explain this apparent change in radio-sensitivity with different fractionation schemes.

Extensive studies have been made of the various factors responsible for changes in the biological effect of radiation with different fractionation schemes. In general an increase in the number of fractions with the same total dose will reduce the biological effect. Strandquist (1944) demonstrated how the cure of squamous carcinoma of the skin and the radiation response in the skin are related to both the total dose and the fractionation. However, other tissues do not seem to follow the same iso-effect curves, for example Regaud's classical experiments on the rabbit testis (Regaud and Ferroux, 1927, 1929).

This reduction in biological effect with increasing numbers of fractions is mainly due to a reduction in the size of individual fractions but also results from a longer treatment period (Fowler, 1968). The mechanisms involved include both repair of sub-lethal damage (Elkind, 1960) and regeneration or repopulation (Lajtha *et al.*, 1960).

In malignant tumours additional factors affect the response to changes in fractionation. In contrast to normal tissues, tumours have little capacity to increase repopulation following loss of cells after radiation. In addition, inadequate vascular proliferation during growth of the tumour gives rise to hypoxic areas which are more resistant to radiation (Gray *et al.*, 1953). Re-oxygenation of these hypoxic cells may occur when some of the cells competing for the oxygen are eliminated by irradiation (Reinhold, 1967; Thomlinson, 1968).

As a result of these factors a few large fractions may achieve greater tumour-cell killing than many small daily fractions, which is still the method in common use. High-dose fractions should result in considerable cell killing, faster repopulation of normal tissues and greater reoxygenation and revascularization of tumour tissues during the longer intervals between fractions. A number of prospective studies have been carried out on patients in this Institute to investigate the influence of different individual doses and fractionation schemes on tumours and normal tissues (Eichhorn *et al.*, 1970, 1972, 1975). This paper reports the results of these investigations in patients with bronchial carcinoma.

MATERIALS AND METHODS

Patients were treated either with high individual doses (400–1,000 cGy (rad)) at intervals of at least five days, or lower individual doses (200–250 cGy (rad)) given five or six times a week. Patients with small, operable tumours were treated pre-operatively to a dose of 5500 cGy and those with larger inoperable tumours were treated to a dose of 7700 cGy. The total time taken for irradiation varied according to the fractionation schemes (see Tables I, II, III). The diagnosis was confirmed histologically in each case by biopsies taken at bronchoscopy.

Since survival is not a direct measure of local tumour response the specimens from operation or autopsy were examined histologically to evaluate the effect of irradiation. Multiple biopsies were taken from all the regions which appeared macroscopically to be still viable and these were examined microscopically. If histological examination revealed only necrosis and scar tissue with no obvious tumour cells present, the tumour was described as being completely destroyed. When foci of tumour cells were seen, even if they were very small, the tumour was considered to be still viable. The percentage of patients showing complete tumour destruction was used as a measure of the effectiveness of irradiation.

The patients with inoperable tumours were initially selected for high-dose irradiation on the basis of the following criteria:

1. The tumour was radiologically and clinically limited to one side of the thorax (including

---

*Part of this paper was presented at the XIV International Congress of Radiology, Rio de Janeiro, 1977.

mediastinum and supraclavicular fossa, involvement of the thoracic wall and damage to the phrenic or recurrent laryngeal nerves).

2. No distant metastases were detectable by routine clinical methods (without using routine radiographs or isotope scans of the skeleton or brain).

3. There was no evidence of a pleural effusion containing malignant cells.

There was, however, selection of patients depending on success in obtaining an autopsy (depending on where they died). Autopsies were performed on 25–50% of patients.

All clinically operable patients were included in the pre-operative irradiation series. The resection rate was 82% and an interval of four weeks was allowed between the end of irradiation and surgery.

Since these investigations were carried out prospectively, but not on a randomized series of patients, a careful comparison was made of the groups. This showed no statistical difference in the distribution of histological types, target volumes or total doses given (Eichhorn *et al.*, 1970, 1972).

RESULTS

The results are shown in Tables I–III. In small operable tumours (Table I) 53% of resected specimens after daily low dose irradiation showed no viable tumour. After high dose irradiation 15% (six out of 39 specimens) were free of tumour. This difference in tumour control is statistically significant ($p < 0.05$) in spite of the fact that the second group had a larger ret dose (Orton and Ellis, 1973).

Patients with larger inoperable tumours (Table II) irradiated daily were free of tumour on autopsy in 29% of cases (31 out of 108). In those irradiated with higher doses every five days only 18% were free of tumour.

When inoperable tumours were treated with one to three large fractions followed after five to ten days by daily small fractions (Table III) 39% (35 out of 90) were histologically free from viable tumour. The difference between those patients receiving large fractions only (group VI) and those receiving one large fraction followed by multiple small fractions (group VII) is statistically significant ($p < 0.05$).

DISCUSSION

In these studies of patients with bronchial carcinoma all the series in which many small fractions were used show a more marked radiation effect on the tumour than those using few large fractions. Differentiation of the tumour, the total dose, the target volume and the NSD value did not influence this result (on the contrary it should have favoured the groups receiving large fractions). The time taken in treating patients with the large fractions was between 40% and 70% longer, but the consequent reduced biological effect would be more than compensated for by the larger individual doses used. If the NSD formula is applied (Orton and Ellis, 1973), irradiation with 11 fractions results in a 30% higher ret dose than with 22–28 fractions. Moreover, lengthening the treatment time from 4 to 28 days results in an increase in tolerance of pig skin treated in five fractions of only 17% (Fowler, 1968).

The reduced effectiveness of large individual fractions may be due to a component of hypoxic cells which do not influence survival to a small dose of 250 cGy and which is progressively eliminated by re-oxygenation between fractions. Another possibility suggested by Regaud's experiments on the rabbit testicle is that the kinetics of the tumour cells in different types of tumour may be the main reason for varying response to different regimes of fractionation.

TABLE I

COMPLETE TUMOUR DESTRUCTION WITH LOW DAILY DOSES COMPARED WITH HIGH DOSES AT LONGER INTERVALS. SMALL OPERABLE TUMOURS.

Group	No. of fractions × dose (cGy)	No. of surgical specimens	No. tumour neg. §	% tumour neg.	total tumour dose (cGy)	total time (days)	NSD (ret)	tumour volume (cm³)	% differentiated tumours
I	22 × 250*	51	27	53	5500	27	1843	74	84
II	4 × 400§ 6 × 600†	23	4	17	4700	46	2045	65	74
III	2 × 1000§‡ 6 × 600†	16	2	13	5500	46	2459	45	63

*six times weekly.
†interval five days.
‡interval eight to ten days.
§histologically.

TABLE II

Complete tumour destruction with low daily doses compared with high doses at longer intervals. Larger inoperable tumours.

Group	No. of fractions × dose (cGy)	No. of autopsies	No. tumour neg.§	% tumour neg.	total tumour dose (cGy)	total time (days)	NSD (ret)	tumour volume (cm^3)	% differentiated tumours
IV	26 × 250*	34	11	32	6500	40	2086	216	67
V	16 × 250†§ 20 × 200†	74	20	27	7700	61	2423	199	68
VI	11 × 590‡	62	11	18	6500	66	2709	188	72

*six times weekly.
†five times weekly with three weeks gap.
‡interval five days.
§histologically.

TABLE III

Complete tumour destruction with one to three high initial doses and subsequent daily low doses. Large inoperable tumours.

Group	No. of fractions × dose (cGy)	No. of autopsies	No. tumour neg.‡	% tumour neg.	total tumour dose (cGy)	total time (days)	NSD (ret)	tumour volume (cm^3)	% differentiated tumours
VII	1 × 600§ 22 × 250†	41	16	39	6250	47	2087	216	59
VIII	1 × 1000*§ 2 × 800*§ 17 × 250†	12	5	41	6800	53	2518	230	75
IX	1 × 400§ 27 × 200†	37	14	38	5700	47	1706	225	73
VII–IX		90	35	40					

*interval eight to ten days.
†five times weekly.
§histologically.

The following hypothesis is suggested. There is a specific ratio between proliferating and non-proliferating compartments in a tumour, which is dependent on the characteristics of the tissue of origin. The normal tissues maintain homeostatic balance between these compartments, compensating for losses from the proliferating compartment by transfer of cells from the non-proliferating reserve pool. After malignant change the equilibrium shifts to a greater or lesser extent, so that a balance between the proliferating and non-proliferating compartments may be maintained for a long period.

Thus, tumours arising from bone marrow or testicular epithelium may be expected to have a relatively large proliferating compartment, whereas tumour of bronchial epithelium will have a small proliferating compartment.

Cells within the proliferating compartment are relatively radiosensitive with a Do of 200–300 cGy for most tissues, according to cell culture experiments. Thus radio-sensitivity will be determined by the size of the proliferating compartment in a tumour, which in turn depends on the tumour type.

Moreover, the failure of hypoxic cells to divide may be offset by recruitment of other cells into the proliferating compartment. Thus it appears that in spontaneous human tumours the size of the proliferating compartments has a greater influence on radio-sensitivity than hypoxia.

The proliferating compartment, depleted by individual doses in the range of the experimental Do, will be restored from the non-proliferating compartment within 24 hours. Tumours with a significant proliferating compartment will thus respond best to daily doses of 200–300 cGy. Higher doses are less efficient as the non-proliferating compartment is more resistant to radiation and fewer fractions can be given.

There are some rare tumours, such as fibrosarcomas, which are composed almost entirely of very slowly dividing cells. These tumours are relatively resistant to low LET radiation and may be affected only by high doses per fraction. This necessitates larger intervals between treatments to permit the recovery of normal tissues, and it may be better to use high LET radiation for these tumours.

The specific balance of the tumour-cell kinetics may finally break down and in a few cases growth may be disorganized from the outset. However, the majority of tumours seem to show only a partial loss of homeostatic control with a change in the equilibrium point between the proliferating and non-proliferating compartments.

To confirm the above results, and to test this hypothesis, two further randomized trials are in progress comparing smaller and larger differences in the fraction size and in the intervals between irradiation.

REFERENCES

EICHHORN, H.-J., LESSEL, A. and JACOB, R., 1970. Der Einfluß unterschiedlicher Einzeldosen und Fraktionierungsrhythmen auf die Rückbildung menschlicher Tumoren. *Strahlentherapie, 140*, 148–155.

EICHHORN, H.-J., LESSEL, A. and ROTTE, K.-H., 1972. Einfluß verschiedener Bestrahlungsrhythmen auf Tumor- und Normalgewebe *in vivo. Strahlentherapie, 143*, 614–629.

EICHHORN, H.-J. and LESSEL, A., 1975. Klinische Untersuchungen über Bedeutung unterschiedlicher Fraktionierungsrhythmen für die Strahlentherapie. *Radiobiologia Radiotherapia, 16*, 437–441.

ELKIND, M. M. and SUTTON, H., 1960. I. Repair of X-ray damage in surviving Chinese hamster cells. *Radiation Research, 13*, 556–593.

FOWLER, J. F., 1968. The rationale of dose fractionation. In *Frontiers of Radiation Therapy and Oncology*, Ed. J. M. Vaeth (S. Karger, Basel/New York), Vol. 3, pp. 6–23.

GRAY, L. H., CONGER, A. D., EBERT, M., HORNSEY, S. and SCOTT, O. L. A., 1953. The concentration of oxygen dissolved in tissues at the time of radiation as a factor in radiotherapy. *British Journal of Radiology, 16*, 638–648.

LAJTHA, L. G., OLIVER, R. and ELLIS, F., 1960. Rationalization of fractionation in radiotherapy. *British Journal of Radiology, 33*, 634–635.

ORTON, C. G. and ELLIS, F., 1973. A simplification in the use of the NSD concept in practical radiotherapy. *British Journal of Radiology, 46*, 529–537.

REGAUD, C. and FERROUX, R., 1927. Discordance des effets des rayons X d'une part dans la peau, d'autre part dans le testicule par le fractionnement de la dose: diminution de l'efficacité dans la peau maintien de l'efficacité dans le testicule. *Comptes rendus des Séances de la Société de Biologie et de ses Filiales* (Paris), *97*, 431–434.

REGAUD, C. and FERROUX, R., 1929. Über den Einfluß des "Zeitfaktors" auf die Sterilisation des normalen und des neoplastischen Gewebes durch die Radiotherapie. *Strahlentherapie, 31*, 495–508.

REINHOLD, H. S., 1967. The postradiation behaviour of transplantable solid tumours in relation to the regional oxygenation. In *Progress in Radiology* (International Congress Series No. 105), Ed. L. Turano, A. Ratti, and C. Biagini, (*Excerpta Medica, Amsterdam*). Vol. 2, pp. 1482–1486.

STRANDQUIST, M., 1944. Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionierung. Erfahrungen aus dem Radiumhemmet an 280 Haut- und Lippenkarzinomen. *Acta Radiologica Supplementum 55*, 1–300.

THOMLINSON, R. H., 1968. Changes of oxygenation in tumours in relation to irradiation. In *Frontiers of Radiation Therapy and Oncology*, Ed. J. M. Vaeth (S. Karger, Basel/New York), Vol. 3, pp. 109–121.

Book review

Radiation Therapy Technology (Examination Review). 814 Multiple Choice Questions and Referenced Explanatory Answers. Ed. J. Stryker, J. A. Clement, D. E. Velkey and C. A. Gruver, pp. 265, 1980 (Medical Examination Publishing Co., New York), £14·00.
ISBN 0–87488–459–1

This is a very useful paperback which not only enables a student to check and improve his knowledge but also helps him to gain experience in the art of answering multiple-choice questions. It covers all the important aspects of radiation therapy training, ranging from anatomy and physiology through diseases of the various systems to radiation safety.

It is far from a simple list of multiple-choice questions with their correct answers indicated numerically, as these are given in brief but adequate detail and referenced.

It is to be recommended to students for basic and higher examinations in radiotherapy and allied branches of medical physics. It also makes useful reading for the established clinician who is interested in teaching.

BRENDAN HALE.

1981, *British Journal of Radiology*, *54*, 136

Scientific note

Brachytherapy build-up factors

By R. O. Kornelsen, Ph.D. and M. E. J. Young, M.Sc.

Division of Radiation Physics, Cancer Control Agency of British Columbia, Vancouver, BC, V5Z 3J3, Canada

(*Received July 1980*)

Webb and Fox (1979) have recently calculated the dose distribution around point γ-ray emitters in water by a Monte Carlo method. It is useful to have such a set of self-consistent data, but for clinical dosimetry an analytical function is more convenient. The radial dependence of dose in a large water medium can be represented by $e^{-\mu r} B/r^2$ where μ denotes the linear attenuation coefficient for the appropriate photon energy and B is a build-up factor. Evans (1955; 1967) has suggested that B may be represented by

$$B = 1 + k_a (\mu r)^{k_b}$$

where k_a and k_b are constants. We have therefore fitted the data of Webb and Fox to the equation $D_r = D_1 e^{-\mu r} \{1 + k_a (\mu r)^{k_b}\}/r^2$ for $r \geqslant 1$ cm (D_1 denotes the dose at 1 cm distance).

It was necessary initially to assign a value of D_1 for each nuclide. It was then possible to evaluate $F = \{r^2 D_r e^{\mu r}/D_1\} - 1$ and fitting a straight line to a plot of log F against log r enabled the constants k_a and k_b to be determined. A revised estimate for the dose at 1 cm was thus obtained and the process repeated. In the second iteration, lines were fitted by the least squares method. The resulting values are given in Table I. Figure 1 shows the data of Webb and Fox from 1 cm to 18 cm compared with the curves calculated from Evans' equation using these constants. The fit for ^{60}Co and ^{137}Cs is excellent. It is not quite so good for the nuclides with complex and/or low energy spectra but is still very acceptable.

TABLE I

Nuclide	μ cm^2 g^{-1}	k_a	k_b
^{60}Co	0.0632	0.896	1.063
^{226}Ra	0.0811	1.17	1.19
^{137}Cs	0.0858	1.14	1.20
^{198}Au	0.105	1.48	1.32
^{192}Ir	0.113	1.59	1.36

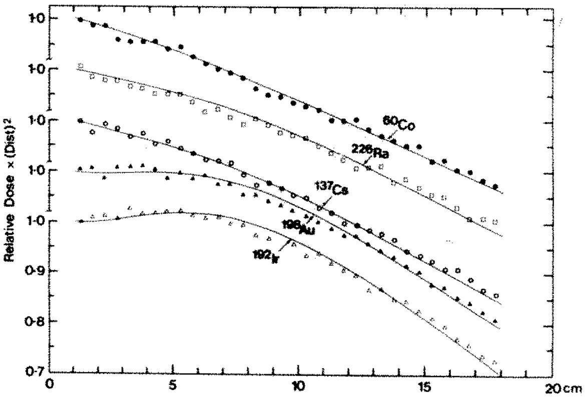


FIG. 1.

Dose distribution around point γ-emitters in water. Points show the Monte Carlo data of Webb and Fox (1979). Lines are calculated from the equation given in the text.

REFERENCES

EVANS, R. D., 1955. *The Atomic Nucleus* (McGraw-Hill, New York), pp. 732–734.

1967. In *Radiation Dosimetry*, Ed. F. H. Attix and W. C. Roesch (Academic Press, New York), p. 151.

WEBB, S. and FOX, R. A., 1979. The dose in water surrounding point isotropic gamma-ray emitters. *British Journal of Radiology*, *52*, 482–484.

1981, *British Journal of Radiology*, *54*, 137–138 FEBRUARY 1981

Technical note

Protective effect of spectacles

By M. J. Day, B.A., Ph.D. and E. Forster, D.C.R., D.H.S.A.

Regional Medical Physics Department, Newcastle General Hospital

(*Received July 1980*)

A recent statement of the International Commission for Radiological Protection (ICRP, 1980) recommends, for non-stochastic effects to the lens of the eye, an annual dose limit of 150 mSv (15 rem), the corresponding value for any other organ being 500 mSv (50 rem). The lower value for the eye implies that under certain circumstances the lens will be the critical organ for formal assessment of radiation hazards. For example, this may well be the case for localized irradiation of the head with X rays (Riley *et al.*, 1972; Wohni and Stranden, 1979). Under these conditions the weighted average dose for the whole body (the "effective dose") may be a small fraction of the maximum local dose. The annual dose limit for local non-stochastic effects then becomes more critical than that for stochastic effects, namely 50 mSv (5 rem).

It is therefore relevant to consider the effect of local shielding of the eyes, since a reduction in dosage below 30% may cause the skin to become the critical organ. In diagnostic radiology commercially available lead-glass spectacles will reduce the dose to the lens to about 10–15% (Bergstrom *et al.*, 1977). Certain flint glasses such as "Hydex" produce comparable X-ray attenuation (Taylor, 1978, personal communication) though photochromic glasses give somewhat less protection (Littleton *et al.*, 1978) than lead glass. Ordinary crown-glass spectacles will also produce some dose reduction and this note reports relevant measurements on such spectacles worn by a small sample of hospital staff.

Measurements were made of the transmission of 62 and 102 kV X rays through 22 unselected pairs of spectacles. In order to allow application to X-ray beams with various combinations of kV and filtration, the results have been expressed in terms of aluminium-equivalent (Table I). For the 21 lenses measured at both 62 kV and 102 kV the aluminium-equivalents averaged 3.60 and 3.71 mm Al respectively. The difference is not significant on a paired t-test ($P=0.16$). As expected, the two pairs of photochromic glasses gave considerably greater than average X-ray attenuation, whereas the attenuation in the one pair of plastic lenses was practically negligible.

The reduction in dosage by localized attenuation of the primary X rays is limited in practice because of backscatter of unattenuated X rays by the surrounding tissues. Measurements were therefore made by TLD using a head phantom fitted with simulated "spectacles" consisting of 2 mm lead discs of about 5 cm equivalent diameter. The surface dose at the eye was found to be reduced to 11% (62 kV) and 13% (102 kV) of the value in the absence of the

TABLE I

TRANSMISSION OF X RAYS THROUGH SPECTACLE LENSES

kV	Total filtration, mm Al	HVT, mm Al	Number of lenses	Transmission (narrow beam). Range and mean	Equivalent thickness mm Al. Range and mean	Dose to lens of eye with backscatter (% of skin dose). Mean value
Ordinary crown glass lenses						
62	3.5	2.29	38	24–56% (40±8%)	1.9–6.1 (3.5±1.0)	46%
102	3.5	3.79	21	37–66% (53±8%)	2.1–6.5 (3.7±1.2)	58%
Photochromic lenses						
62	3.5	2.29	4	11–23% (15%)	6.3–10.7 (9.1)	24%
102	3.5	3.79	4	23–37% (30%)	6.5–10.5 (8.9)	38%

lead discs. These results agree well with calculations using the following formula, setting $T=0$ since penetration through the lead discs was negligible.

Percentage dose to eye =

$$100-(100-T)\ \mathrm{BSF}(D_2)/\mathrm{BSF}(D_1)$$

where T = percentage X ray transmission through shield; $\mathrm{BSF}(D)$ = backscatter factor for field of diameter D; D_1, D_2 = equivalent diameters of head (frontal view) and of protective shield respectively.

The dose to the eye is expressed as a percentage of the dose at the same point in the absence of the shield. Backscatter factors were taken from *BJR Supplement 11* (1968).

The experimental values of T enable estimates to be made of the overall protective effect of actual spectacles—see last column of Table I. The mean value for typical diagnostic X rays is about 50%. Corresponding mean values for γ rays are 87% ($^{99}\mathrm{Tc}^{\mathrm{m}}$) and 91% ($^{131}\mathrm{I}$).

The possible criticality of eye dosage has been studied by Wohni and Stranden (1979) for simulated fluoroscopy examinations in which the "radiologist" wore a lead apron. They found that using the contemporary annual dose limit (ICRP, 1977) of 300 mSv (30 rem) eye dosage was usually more critical than whole-body dosage. However, Gill *et al.* (1980), using the same data but taking greater account of dosage to the head, conclude that the whole-body dose is more critical. The apparent inconsistency appears to arise in calculation of the effective dose using different interpretations of the "remainder", *i.e.* the five organs or tissues (other than the six specified tissues) which received the highest dosage (ICRP, 1977). Other authors (Bushong, 1970; Cruikshank *et al.*, 1980) have suggested that, in various radiological procedures, the finger dose may be more critical, even though no account was taken of enhanced X-ray absorption in bone mineral. With probable developments in technique it seems that no final statement can be made on whether local dosage to the eye, skin or extremities is more critical than whole-body dosage.

Our results imply that the protective effect of ordinary glasses worn by radiologists and radiographers might not be sufficient to prevent the lens of the eye being the critical organ. Some additional protection would then be required and the question arises as to how this should be provided. Bearing in mind the unavoidably rather arbitrary basis of the ICRP dose limits, we believe that the use of protective glasses for selected individuals may be encouraged. However it is important that such usage should not induce complacency about the doses to skin and bone and efforts should be made to keep these well below the 500 mSv/year (50 rem/year) level at which such questions become pertinent.

It may be noted that the wearing of glasses is only marginally relevant to protection against stochastic effects of radiation since the reduction in the effective whole-body dose afforded even by lead glass spectacles does not exceed a few per cent and can be considered negligible for practical purposes. Consequently these results are directly relevant only if the dosage is considerably larger than is commonly the case in diagnostic radiology.

ACKNOWLEDGMENTS

The authors wish to acknowledge the support and encouragement of Professor K. Boddy. They are grateful to Miss K. Ayre and Miss K. Copeland for technical assistance.

REFERENCES

Bergstrom, K., Jorulf, H. and Lofroth, P.-O., 1977. Eye lens protection for radiological personnel. *Radiology, 124*, 839–840.

British Journal of Radiology, 1968. Central axis depth dose data for use in radiotherapy. Ed. M. Cohen *et al.*, *British Journal of Radiology, Supplement 11.*

Bushong, S. C., 1970. Radiation control in diagnostic roentgenology, *Health Physics, 19*, 557–561.

Cruikshank, J. G., Fraser, G. M. and Law, J., 1980. Finger doses received by radiologists during Chiba needle percutaneous cholangiography, *British Journal of Radiology, 53*, 584–585.

Gill, J. R., Beaver, P. F. and Dennis, J. A., 1980. Proceedings of the 5th International Congress of the International Radiation Protection Association, Jerusalem (Pergamon Press, Oxford, in press).

ICRP, 1977. Recommendations of the International Commission on Radiological Protection (ICRP Publication 26).

ICRP, 1980. Statement and Recommendations of the International Commission on Radiological Protection.

Littleton, J. T., Durizch, M. L. and Perry, N., 1978. Radiation protection of the lens for patients and users. *Radiology*, 129, 795–798.

Riley, R. C., Birks, J. W., Palacios, E. and Templeton, A. W., 1972. Exposure of radiologists during special procedures, *Radiology, 104*, 679–683.

Wohni, T. and Stranden, E., 1979. The new ICRP concept of person-dose related to the film-badge exposure for some geometries and radiation qualities used in medical X-ray. *Health Physics, 35*, 71–73.

1981, *British Journal of Radiology*, *54*, 139–140 FEBRUARY 1981

Case reports

Transgression of localizing wire into the pleural cavity prior to mammography

By *J. B. Bristol, F.R.C.S., and P. A. Jones, M.R.C.P., F.R.C.R.

Departments of Surgery and Radiology, Royal United Hospital, Bath BA1 3NG

(*Received August 1980*)

The advent of mammography has created the need to localize impalpable breast lesions prior to excision biopsy. Among the methods described is percutaneous needle insertion (Threatt *et al.*, 1974). The Frank needle consists of 9·5 cm 25-gauge wire with an acutely angled tip lying inside a 9 cm hollow needle (Fig. 1). This assembly is inserted into the breast under local anaesthesia until the tip is judged to be near the area in question. The needle is withdrawn, leaving the wire fixed in position by its hooked end, and its relation to the suspicious mass checked by further X-ray prior to biopsy (Frank *et al.*, 1976). We report a case in which movement of the wire resulted in its passage into the pleural cavity.

CASE REPORT

The patient was a 56-year-old housewife whose left breast revealed a suspicious area on mammography performed during a screening programme. Both breasts were large and this area proved impalpable. On her subsequent admission for biopsy, a further mammogram was performed, demonstrating a mass deep in the breast. A Frank needle was inserted as described above, leaving 5 cm protruding from the skin. On being asked to sit up, the patient moved abruptly, and immediately complained of severe left chest and arm pain, and became dyspnoeic. Examination showed that the wire had retracted into the breast. Because of the siting of the mammography unit relative to the hospital where biopsy was to be performed, a three-mile ambulance journey was required to bring the patient to theatre. Her pain and dyspnoea persisted. An X-ray confirmed that the wire was still present with no pneumothorax. Under general anaesthesia the area was explored using image intensifier control. A short search of the breast did not reveal the wire and screening showed it moving freely with each respiration indicating its presence within the pleural cavity. On performing a left lateral thoracotomy the wire was retrieved from the posterior part of the pleural cavity with no lung damage apparent. Following chest closure, a mass corresponding to the area seen on the mammogram was excised and subsequent histology proved it to be benign. The patient's recovery was uneventful.

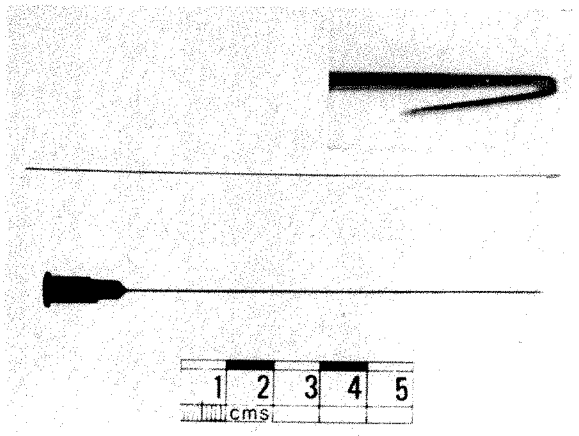


FIG. 1.
Needle and wire assembly. Inset: end of wire showing hook.

DISCUSSION

In this patient it seems that the wire with its hooked end deep in the breast was propelled into the pleural cavity by the patient's sudden movement on sitting up. Alternatively, it may have already engaged the pectoral muscle and been squeezed into the chest by muscle contraction. Once the tip was in each respiratory movement would tend to pull it further aided by the hooked end which also prevented its extrusion. The delay caused by the ambulance journey may have allowed time for the whole wire to traverse the chest wall, but this is speculative.

Percutaneous needle or wire localization of impalpable breast lesions was developed because non-invasive methods such as the use of skin markers (Frankl and Rosenfeld, 1975) or extrapolations onto a map of the breast (Stevens and Jamplis, 1971) are insufficiently accurate especially in large breasts which are distorted by the compression applied during mammography. The technique is hitherto free of reported complications. Both the paper of Frank *et al.* and that of Jensen and Luttenegger (1979) stress the importance of the hooked end in avoiding displacement and although the former authors state in a footnote that retraction of the anchored guide wire into the breast may occur following compression during mammography, they do not advocate any precaution other than keeping it sterile and unshortened. Our experience suggests that it is wise to guard the protruding end.

---

*Present address, to which all correspondence re this paper should be sent: Department of Surgery, Bristol Royal Infirmary, Bristol BS2 8HW

1981, *British Journal of Radiology*, *54*, 140–142

ACKNOWLEGMENT

We thank Mr. K. Lloyd-Williams, Consultant Surgeon, for permission to report this complication.

REFERENCES

FRANK, H. A., HALL, F. M. and STEER, M. L., 1976. Preoperative localization of nonpalpable breast lesions demonstrated by mammography. *New England Journal of Medicine*, *295*, 259–260.

FRANKL, G. and ROSENFELD, D. P., 1975. Xeroradiographic detection of occult breast cancer. *Cancer*, *35*, 542–548.

JENSEN, S. R. and LUTTENEGGER, T. J., 1979. Wire localization of nonpalpable breast lesions. *Radiology*, *132*, 484–485.

STEVENS, G. M. and JAMPLIS, R. W., 1971. Mammographically directed biopsy of nonpalpable breast lesions. *Archives of Surgery*, *102*, 292–295.

THREATT, B., APPELMAN, H., DOW, R. and O'ROURKE, T., 1974. Percutaneous needle localization of clustered mammary microcalcifications prior to biopsy. *American Journal of Roentgenology*, *121*, 839–842.

Upward dislocation of the first rib: a rare cause of nerve entrapment, producing brachialgia

By *C. C. McCormick, F.R.C.R., M.R.A.C.R., †S. S. Gubbay, M.D., F.R.A.C.P. and ‡J. S. Lekias, F.R.A.C.S.

Departments of *Radiology, †Neurology, and ‡Neurosurgery, Royal Perth Hospital, Perth, Western Australia

(*Received August 1980*)

CASE REPORT

A 50-year-old male presented in February, 1976 with a 2½ year history of pain in the right shoulder and numbness in the right little and ring fingers. He complained of occipital and vertex headaches and pain and swelling in the right side of the throat aggravated by lying on the left side. He had histologically proven multiple subcutaneous lipomata. Initial physical examination revealed right supraclavicular tenderness and superficial sensory loss over the right little and ring fingers with impaired vibratory and position sense loss in the little finger.

Electromyographic examination revealed denervation patterns in the right abductor digiti minimi (ADM) and abductor pollicis brevis (APB) with reduction of both the right ulnar orthodromic sensory potential at the wrist to 5 μV and the mixed conduction at the elbow to 29 μV but without impairment of motor conduction in any segment from Erb's point to ADM. Division of the right scalenus anterior muscle on March 1976 did not relieve his symptoms. Myelography in October 1976 was negative although the cerebrospinal fluid protein level was elevated to 0·61 g/dl.

His symptoms gradually progressed and in January 1979 examination revealed even greater right supraclavicular and also lower cervical tenderness. He had no muscular wasting nor weakness and only the right triceps jerk was depressed. There was mild sensory loss from segments C.5 to T.2 especially in the medial two digits of the right hand.

Electromyograms on this occasion showed possible denervation of the right deltoid, biceps brachii and brachioradialis, and not of APB or ADM. The right median nerve motor and sensory conductions and the right ulnar nerve motor conductions were normal. The right ulnar orthodromic sensory potential at the wrist was reduced to 3 μV and the mixed potential at the elbow to 28 μV. As on the initial assessment it was felt that the patient had a compressive brachial plexopathy.

Radiological findings

Previous radiographs of the cervical spine, thoracic outlet and chest, and a cervical myelogram, had been reported as normal. A CT scan was performed (Fig. 1). This suggested that the neck and head of the right first rib lay at the level of the C.8 intervertebral foramen instead of its usual more caudal position. There was no rotation or scoliosis to account for this asymmetry. Review of the AP radiograph of the cervical spine (Fig. 2) confirmed this upward dislocation of the first rib, and this was more clearly demonstrated in a frontal radiograph taken with cranial angulation of the X-ray beam (Fig. 3).

Operative findings and post-operative follow-up

Through a posterior approach, a longitudinal incision was made from C.6 to T.2 and the first rib was identified and confirmed to be dislocated upwards. The neck and head of the first rib, together with part of the transverse process of the first thoracic vertebra, were resected.

Following surgery a rapid improvement in the patient's symptoms occurred and eight weeks after operation he reported that he was symptom-free apart from minor tingling at the ulnar side of the right wrist.

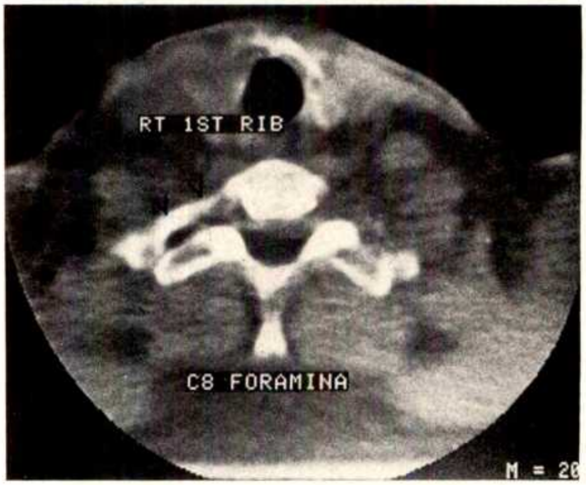


FIG. 1.

CT scan through C.8 foramina. The head and neck of the right 1st rib (arrow heads) is shown to be abnormally situated. There is no significant rotation. The left 1st rib is not visible at this level.

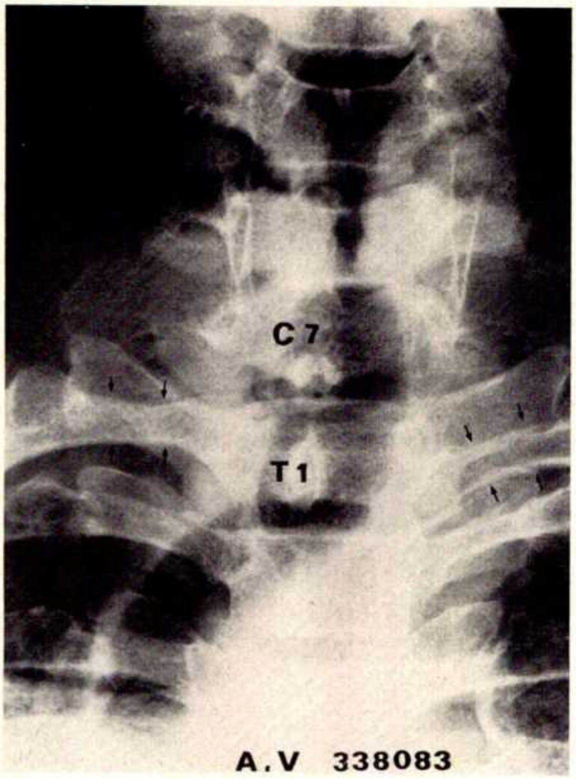


FIG. 2.
AP cervico-thoracic spine. The neck of the 1st ribs (arrowed) are demonstrated to lie at different levels.

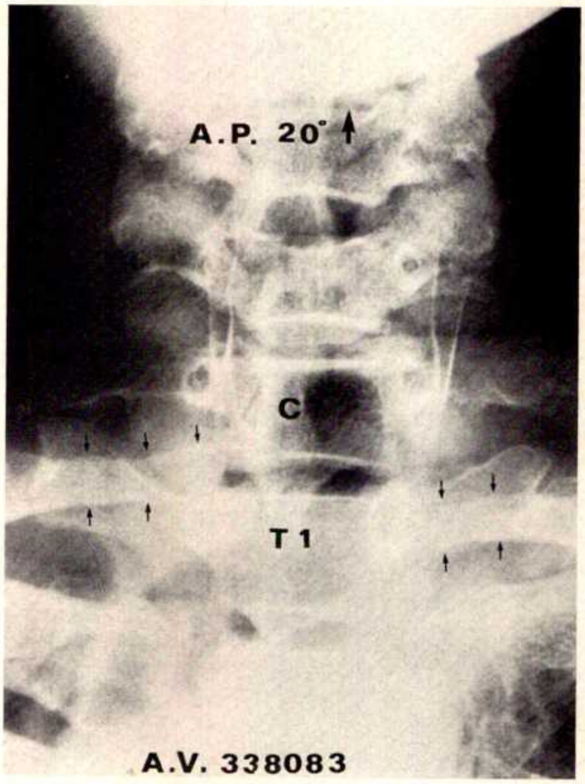


FIG. 3.
AP radiograph of the cervico-thoracic junction angled up twenty degrees. The head of the right 1st rib lies well above its normal situation at the level of the C.7—T.1 disc.

DISCUSSION

Pain and dysaesthesia affecting the neck and upper limb is a common isolated complaint, which may be accompanied by paresis and vasomotor and trophic changes of the arm and hand. The peripheral nerves supplying the upper limb may be vulnerable to entrapment at a number of points along their course through the cervical root canals, the thoracic outlet and the axilla. The major arteries and veins serving the upper limb are closely related to the nerve structures at the thoracic outlet and symptoms of ischaemia and/or venous obstruction may accompany the neurological findings, or present in isolation. A comprehensive account of the compressive syndromes of the thoracic outlet is given in the excellent monograph by Lord and Rosati (1971).

The history and physical findings, together with electromyographic (EMG) examination, are most helpful in the initial assessment of the site of nerve compression. The range of diagnostic possibilities will be further narrowed by radiological examination of the cervical spine and thoracic inlet. By far the commonest cause of a purely neurological lesion is cervical root compression by osteophytes associated with cervical spondylosis (Mayfield, 1975).

Cervical ribs (Halsted and Reid, 1916) have long been recognized as a source of nerve and/or vascular compression, though the association of their presence with signs of neurovascular entrapment is not a simple one. In a significant proportion of patients exhibiting the costoclavicular syndrome, an old fracture of the clavicle can be demonstrated (Mayfield, 1975). Congenital anomalies about the cervico-thoracic junction, including the first thoracic rib (Walshe *et al.*, 1944), may also be associated with entrapment syndromes. The superior pulmonary sulcus tumour (Pancoast, 1932) commonly presents with symptoms and signs in the arm, and hand and early signs of bone erosion should be carefully sought in older patients. Aneurysm of the subclavian artery normally requires arteriography for confirmation. Very rarely pulmonary apical inflammatory lesions may be associated with involvement of the neurovascular bundle at the thoracic outlet. The group of

1981, *British Journal of Radiology*, *54*, 142–144

patients whose symptoms are due to scalenus anticus syndrome (Adson and Coffey, 1927), hyperabduction syndrome (Wright, 1945) or brachial neuritis will usually show no abnormality at radiographic examination.

The first clue to the underlying cause of this patient's symptoms was given by CT study of the cervico-thoracic junction. The upward dislocation of the right first rib was visible on the current and previous radiographs but the asymmetry was minimal in the commonly used projections and was shown unequivocally only by utilizing a "Lordotic" view, *i.e.* an AP radiograph with cranial beam angulation. No significant history of trauma was elicited, even in retrospect. To the best of our knowledge, this cause of thoracic outlet nerve entrapment has not been reported previously.

REFERENCES

Adson, A. W., and Coffey, J. R., 1927. Cervical rib; method of anterior approach for relief of symptoms by division of scalenus anticus. *Annals of Surgery*, *85*, 839–957.

Halsted, W. S. and Reid, M. R., 1916. An experimental study of circumscribed dilatation of an artery immediately distal to a partially occluding band and its bearing on the dilatation of the subclavian artery observed in certain diseases of cervical rib. *Journal of Experimental Medicine*, *24*, 271–286.

Lord, J. W. and Rosati, L. M., 1971. Thoracic-outlet syndromes. *Clinical Symposia*, *23*, (No. 2) (CIBA Pharmaceutical Company, Summit, N.J.).

Mayfield, F. H., 1975. Neural and vascular compression syndromes of the shoulder girdle and arms. In *Handbook of Clinical Neurology*, Ed. P. J. Vinken and G. W. Bruyn. Vol. 7, pp. 430–446 (North Holland Publishing Co., Amsterdam/American Elsevier Publishing Co., New York).

Pancoast, H. K., 1932. Superior pulmonary sulcus tumor. Tumor characterised by pain, Horner's syndrome, destruction of bone and atrophy of the hand muscles. *Journal of the American Medical Association*, *99*, 1391.

Walshe, M. M. R., *et al.*, 1944. On some pressure effects associated with cervical and rudimentary and "normal" first ribs and the factors entering into their causation. *Brain*, *57*, 141–177.

Wright, J. S., 1945. The neuro-vascular syndrome produced by hyperabduction of the arm. *American Heart Journal*, *29*, 1–19.

A fibrovascular polyp of the oesophagus

By *Y. Barki, M.D., †H. Elias, M.D., †F. Tovi, M.D., and *J. Bar-Ziv, M.D.

Departments of *Radiology and †Otolaryngology, Soroka Medical Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer-Sheva, Israel

(*Received August 1979 and in revised form August 1980*)

Benign tumours of the oesophagus are relatively uncommon while squamous carcinoma occurs more frequently. Our series of 38 oesophageal tumours collected over 17 years revealed five benign tumours and 33 carcinomas. Benign tumours constitute 20% of all oesophageal neoplasms (Attah and Haydu, 1968). Because of their slow growth they do not become clinically manifest. Many of them are diagnosed at post-mortem studies with an incidence of 0.5% (Ming, 1973).

Love (1972) found 392 cases of benign oesophageal tumours in his review of literature. Leiomyomas, polyps, cysts, haemangiomas, lipomas, neurofibromas, papillomas and adenomas are the most commonly reported benign growths. Stout and Lattes (1957) prefer not to give exact figures on the histological frequency of the different benign oesophageal tumours. They classified them according to their location as: intraluminal, intramural and extramural.

Leiomyomas are mostly intra and extramural while polyps appear predominantly as intraluminal tumours. Pedunculated lipomas and occasionally pedunculated leiomyomas are encountered with intraluminal localization (Love, 1972; Nora, 1964; Liliequist and Wiberg, 1974). Liliequist and Wiberg noted 160 pedunculated tumours in the literature.

The following is a case report of an unusual benign oesophageal tumour.

CASE REPORT

A 60-year-old male presented complaining of a bolus-like sensation in his throat, progressive dysphagia, intermittent attacks of vomiting and regurgitation of a solid mass into the mouth. Recently he developed dyspnoea while lying on his right side.

Reprint requests to: Jacob Bar-Ziv, M.D., Department of Radiology, Soroka Medical Center, P.O. Box 151, Beer-Sheva, Israel.

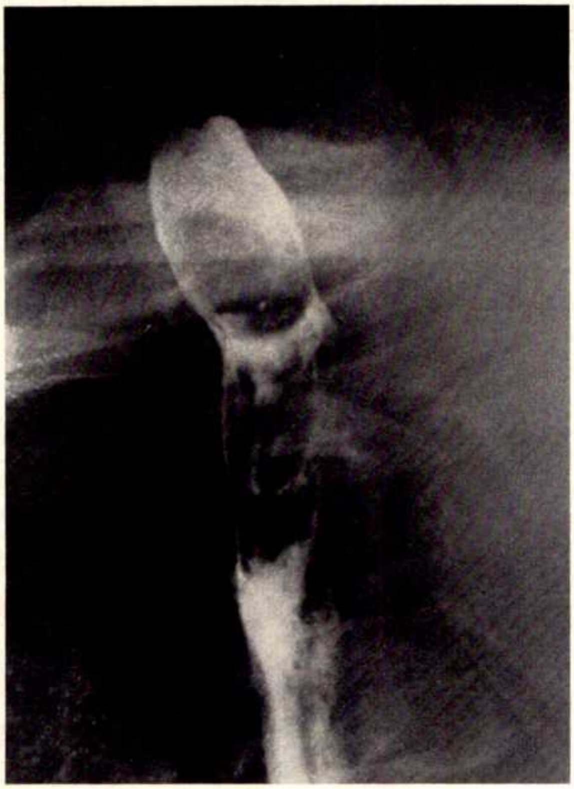


FIG. 1A.

The oesophagogram demonstrates the presence of an intraluminal bilobulated polyp with smooth borders.

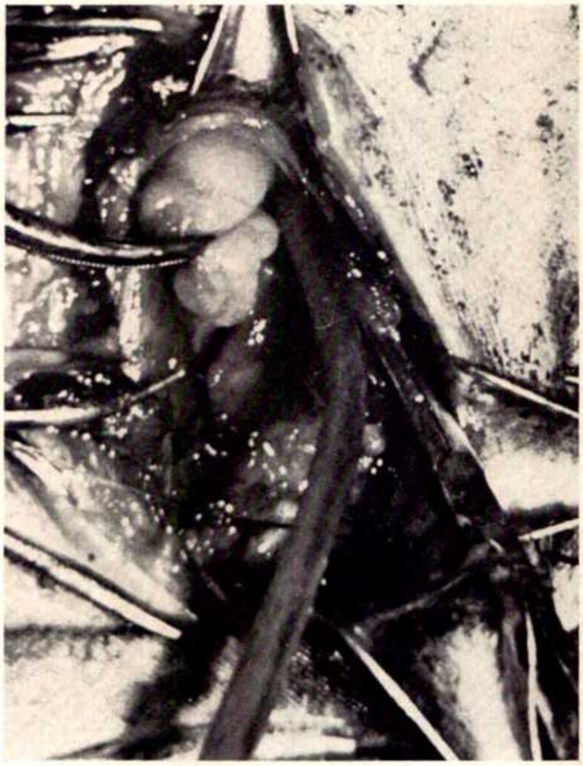


FIG. 1B.

The fibrovascular polyp before excision.

Routine physical examination and laboratory data were normal. The patient was able to regurgitate the solid mass into his mouth for the clinician.

Fluoroscopy using barium as contrast medium revealed an intraluminal, bilobulated oesophageal tumour of 6 cm in length, originating at the level of the cricoid cartilage. Its attachment to the oesophageal wall could not be clearly identified. Its surface was smooth, giving free passage to the distal flow of barium (Fig. 1A).

In view of the pedunculated tumour demonstrated radiologically, surgical excision was undertaken. A paraoesophageal surgical approach permitted excision of a bilobulated solid tumour (Fig. 1B).

The tumour originated from the proximal oesophagus and the left pyriform sinus. Histology showed a fibrovascular polyp (Fig. 2). The patient made an uneventful recovery and remains symptom-free.

DISCUSSION

Submucosal polyps are the second most common benign oesophageal tumours and they present as a pedunculated intraluminal mass (Love, 1972). Rarely they are sessile. Depending on their histological features they could be termed fibromas, fibrolipomas, fibrovascular polyps or lipomas (Jang *et al.*, 1969). In the presence of mixed architecture they may be called hamartomas (Fuller, 1969). The normal mucosal covering of polyps may ulcerate. They are usually of a benign nature. Malignant degeneration is rare, but has been described (Stout and Lattes, 1957).

The ability to regurgitate a high oesophageal tumour is characteristic of a pedunculated polyp. This feature favours a benign nature of the tumour (Liliequist and Wiberg, 1974).

The clinical history coupled with the radiological features of an intraluminal growth or lobulated mass is almost pathognomonic of fibrovascular polyp.

1981, *British Journal of Radiology*, *54*, 144–146

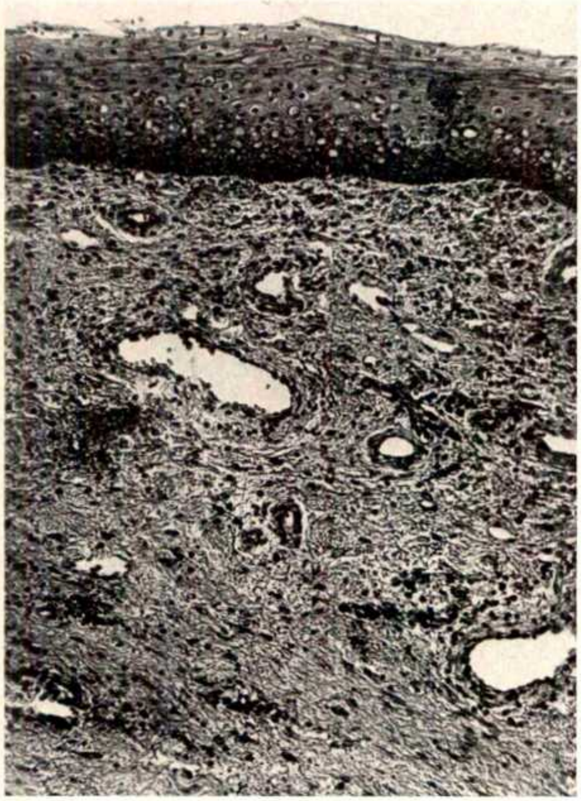


FIG. 2.

Fibrovascular structure of the polyp covered by intact oesophageal mucosa (H. and E. × 125).

ACKNOWLEDGMENTS

We should like to thank Mr. G. H. Gottfried, our photographer, and Mrs. Bilha Savell for her secretarial help.

REFERENCES

ATTAH, E. B. and HAYDU, S. I., 1968. Benign and malignant tumours of the esophagus at autopsy. *Journal of Thoracic and Cardiovascular Surgery*, *55*, 396–404.

FULLER, A. P., 1969. Pedunculated hamartoma of the esophagus. *Journal of Laryngology and Otology*, *77*, 706–713.

JANG, G. C., CLOUSE, M. E. and FLEISCHNER, F. G., 1969. Fibrovascular polyp—a benign intraluminal tumour of the esophagus. *Radiology*, *92*, 1196–1200.

LILIEQUIST, B. and WIBERG, A., 1974. Pedunculated tumors of the oesophagus. Two cases of lipoma. *Acta Radiologica Diagnosis*, *15*, 383–392.

LOVE, W. C., 1972. *Neoplasms of the gastrointestinal tract.* (Hans Haber, Bern/Stuttgart/Vienna), pp. 64–68.

MING, SI-CHUN, 1973. *Atlas of Tumor Pathology.* 2nd series, Fascicle 7. *Tumors of the esophagus and stomach.* (Armed Forces Institute of Pathology, Washington, DC), pp. 17–18.

NORA, P. F., 1964. Lipoma of the esophagus. *American Journal of Surgery*, *108*, 353–356.

STOUT, A. P. and LATTES, R., 1957. *Atlas of tumor pathology*. Fascicle 20. *Tumors of the esophagus* (Armed Forces Institute of Pathology, Washington DC), pp.25–32.

Lymphoma of the colon detected by CT

By J. Hildell, M.D., U. Nyman, M.D. and J.-E. Rosengren, M.D.

Department of Diagnostic Radiology, Malmö General Hospital, University of Lund, S-214 01 Malmö, Sweden

(*Received September 1980*)

The diagnosis of gastrointestinal lesions is usually established by means of radiographic barium studies and endoscopy. Occasionally such lesions may be detected at CT-examinations (Parienty *et al.*, 1979). This report describes a case of lymphoma in the colon detected by CT.

CASE REPORT

A 65-year-old man was operated with excision of a large tumour of the stomach in 1977. At surgery large mesenteric lymph nodes were found. Histologic examination of the tumour revealed a poorly differentiated diffuse lymphocytic lymphoma. A pre-operative double contrast examination of the colon demonstrated two small polypoid lesions in the caecum. Biopsy specimens via colonoscopy showed non-specific inflammatory changes. The patient received radiation and chemotherapy.

In January 1980 abdominal CT was performed as a routine control. Clinically the patient was in complete remission and had no symptoms. The CT-examination revealed no abnormal changes except for a homogeneous lobulated mass 10 cm long and 5 cm in diameter extending from below the liver into the right fossa (Fig. 1A). The mass was thought to originate in the right colon. Two hours later, at repeat examination, there was irregular filling of the mass by contrast medium, given orally prior to the examination (Fig. 1B). Double contrast examination of the colon and small bowel verified the suspicion of lymphomatous involvement of the colon (Fig. 2A, B).

At follow-up examination with CT two months later after intensified chemotherapy the mass had increased in size (Fig. 3).

DISCUSSION

Clinical evidence of secondary lymphomatous involvement of the gastrointestinal tract occurs in 15% of patients with known lymphoma (Wang and Petersen, 1956). The stomach and small bowel are

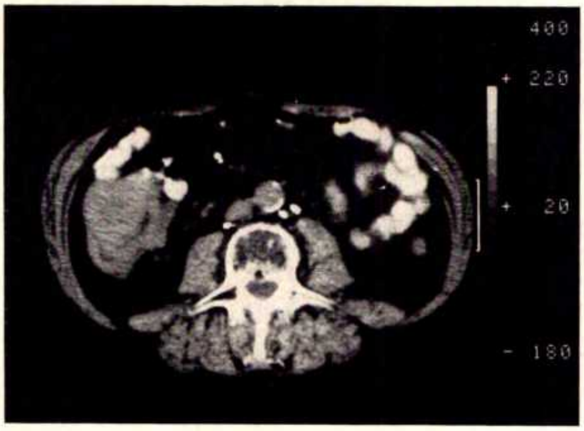


FIG. 1A.
Large lobulated mass in the right fossa at the level of the ileocaecal valve.

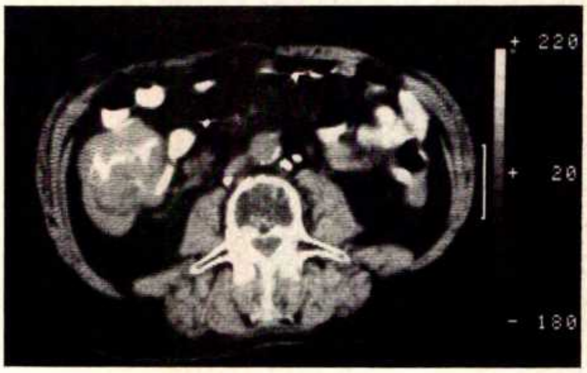


FIG. 1B.
The mass filled with orally administered contrast medium two hours later.

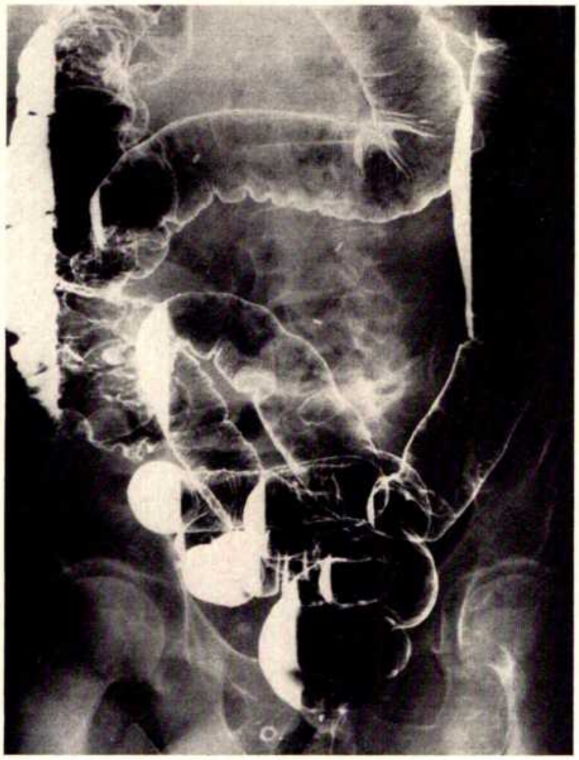


FIG. 2A.
Double contrast examination of the colon. Multiple polypoid lesions in the caecum, ascending, descending and sigmoid colon.

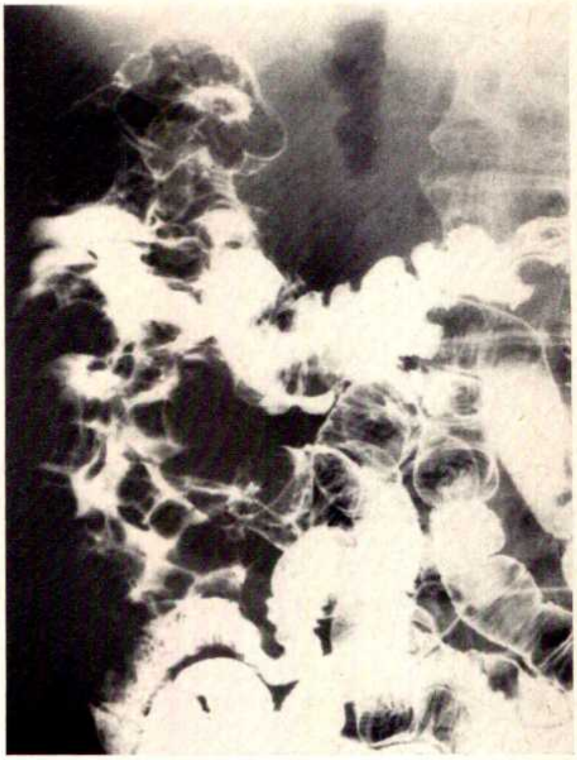


FIG. 2B.
Double contrast examination of the small bowel. Contrast filling of the right colon with multiple filling defects in connection with an intact mucosa—typical for colonic lyphoma.

1981, *British Journal of Radiology*, *54*, 146–148

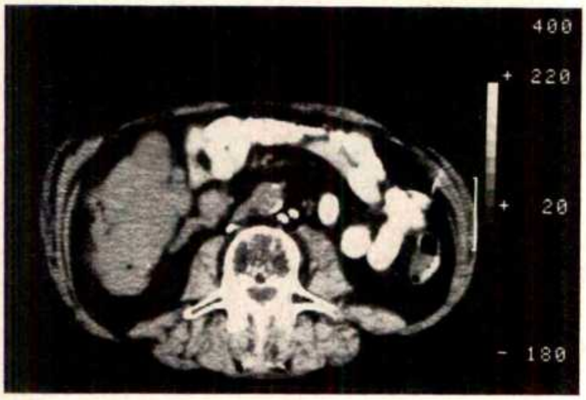


FIG. 3.

Follow-up CT examination two months later with increase in size of the colonic mass.

the most common regions affected (Bush and Ash, 1969; Jones *et al.*, 1973). Secondary colonic involvement is, however, more common than generally appreciated but the diagnosis is seldom made antemortem (Rosenberg *et al.*, 1961). Correct diagnosis is of importance as it alters staging, treatment and prognosis.

In the case presented in this report the patient had no symptoms and the colonic involvement and the CT-findings were accidental. The lymphomatous involvement of the right colon appeared at CT as a marked diffuse thickening of the bowel wall with sharp demarcation from the perivisceral fat and compression of the contrast-filled lumen.

Although CT is not the primary diagnostic modality in the diagnosis of gastrointestinal tumours, such lesions can be demonstrated at CT (Kressel *et al.*, 1978; Lee *et al.*, 1979; Parienty *et al.*, 1979). By filling the bowel lumen with contrast medium the wall of the bowel can be seen as a soft tissue density between the contrast-filled lumen and perivisceral fat. Alterations in thickness of the bowel wall and tumour extension outside the bowel may be detected by CT. Since abdominal CT is frequently used for staging lymphoma the gastrointestinal tract should be scrutinized for lymphomatous involvement. Furthermore, CT was also of value in monitoring the response to radiation and chemotherapy in the present case where progression could be demonstrated despite intensified chemotherapy.

REFERENCES

BUSH, R. S. and ASH, C. L., 1969. Primary lymphoma of the gastrointestinal tract. *Radiology*, *92*, 1349–1354.

JONES, S. E., FUKS, Z., BULL, M., DORFMAN, R., KAPLAN, H., ROSENBERG, S. and KIM, H., 1973. Non-Hodgkin's lymphomas: clinicopathologic correlation in 405 cases. *Cancer*, *31*, 806–823.

KRESSEL, H., CALLEN, P., MONTAGNE, J-P., KOROBKIN, M., GOLDBER, H., MOSS, A., ARGER, P. and MARGULIS, A., 1978. Computed tomographic evaluation of disorders affecting the alimentary tract. *Radiology*, *129*, 451–455.

LEE, K. R., LEVINE, E., MOFFAT, R. E., BIGONGIARI, L. R. and HERMRECK, A. S., 1979. Computed tomographic staging of malignant gastric neoplasms. *Radiology*, *133*, 151–155.

PARIENTY, R. A., SMOLARSKI, N., PRADEL, J., DUCELLIER, R. and LUBRANO, J. M., 1979. Computed tomography of the gastrointestinal tract: lesion recognition and pitfalls. *Journal of Computer Assisted Tomography*, *3*, 615–619.

ROSENBERG, S. A., DIAMOND, H. D., JASLOWITZ, B. and CRAVER, L. F., 1961. Lymphomosarcoma: a review of 1269 cases. *Medicine* (Baltimore), *40*, 31–42.

WANG, C. C. and PETERSEN, J. A., 1956. Malignant lymphoma of the gastrointestinal tract: roentgenographic considerations. *Acta Radiologica Diagnosis*, *46*, 523–532.

Unusual ophthalmic metastasis from a bronchial carcinoma

By S. Scavdis, G. Tritakis and G. Ramantanis

Departments of Ophthalmology and Radiology, General State Hospital of Athens

(*Received March 1980 and in revised form June 1980*)

Metastatic neoplasms of the eye are fairly common and are usually derived from the breast, lung, kidney, prostate or intestine (Bloch and Gartner, 1971; Ferry and Font, 1974). The increased incidence noticed recently might be due to a corresponding increase in the incidence of primary bronchogenic neoplasms (Reese, 1976).

An unusual case of an asymptomatic pulmonary carcinoma with secondary deposit in the iris of the left eye is reported.

CASE REPORT

A 69-year-old man was admitted to hospital because of decreased vision and pain in his left eye for about three weeks.

On clinical examination he had decreased vision of the left eye (7/10), a clear cornea and congested conjunctiva. There was a pale mass over the iris from the 9 to 11 o'clock position with vascularization. The intraophthalmic pressure was 20 mmHg. The patient refused any further investigation and treatment. Two months later he was readmitted because of low visual acuity and severe pain. On examination the mass was then occupying the whole iris and ciliary body and the intraocular pressure was 55 mmHg. A chest X-ray showed the presence of a coin lesion in the right upper zone and tomography confirmed hilar gland enlargement (Figs. 1 and 2). Repeated sputum cytology was negative, but cytological examination of material taken with a flexible broncoscope showed class IV cells. An enucleation of the eye was performed and histological examination showed an

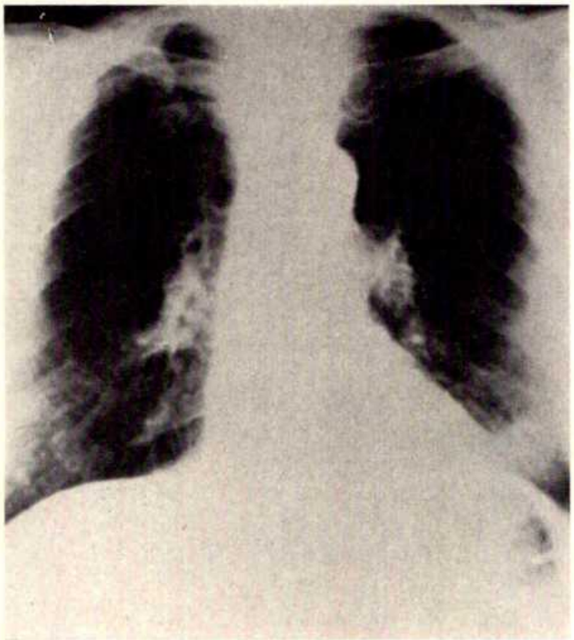


FIG. 1.
Plain chest X-ray showing a coin shadow over the right subclavicular area.

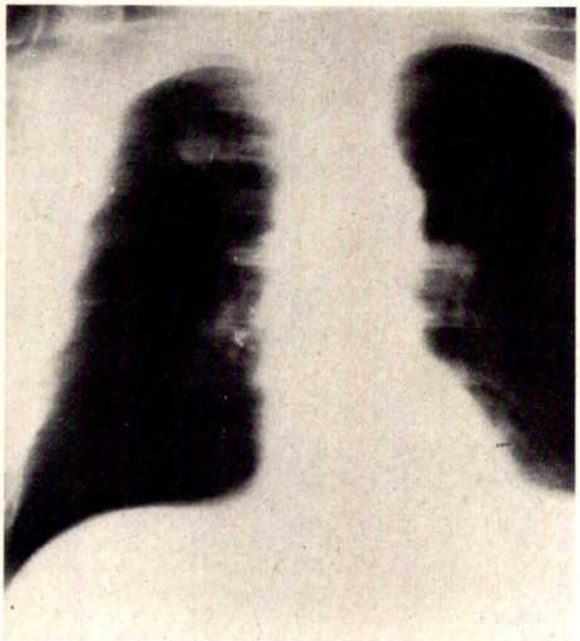


FIG. 2.
Tomography showing hilar gland involvement.

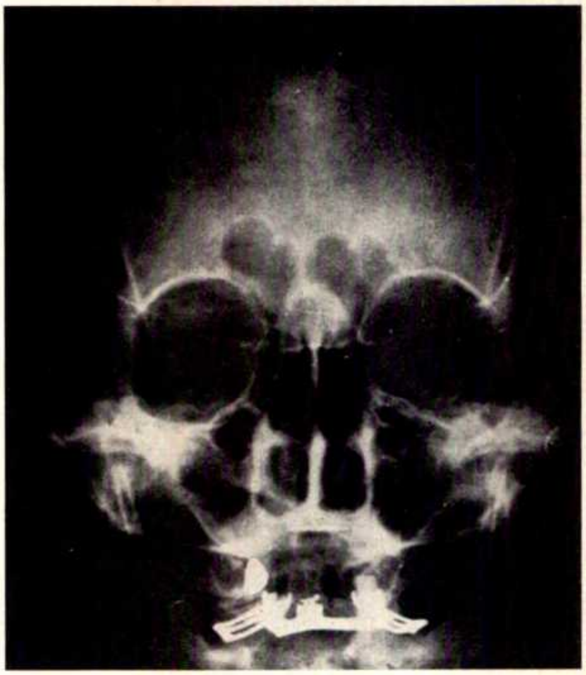


FIG. 3.
Plain orbit X-ray showing no metastatic involvement of bone.

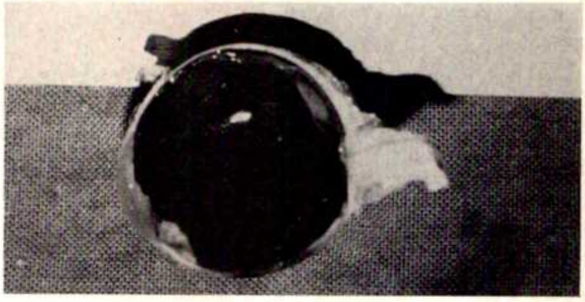


FIG. 4.
View of the left eye where the tumour can be seen occupying the anterior segment (sagittal section).

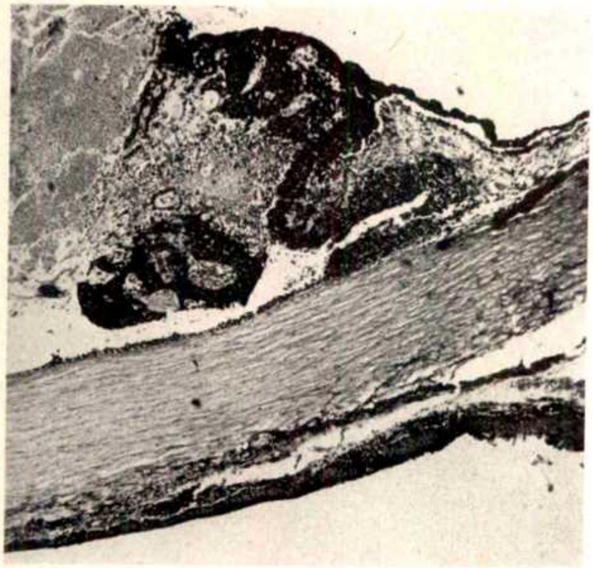


FIG. 5.

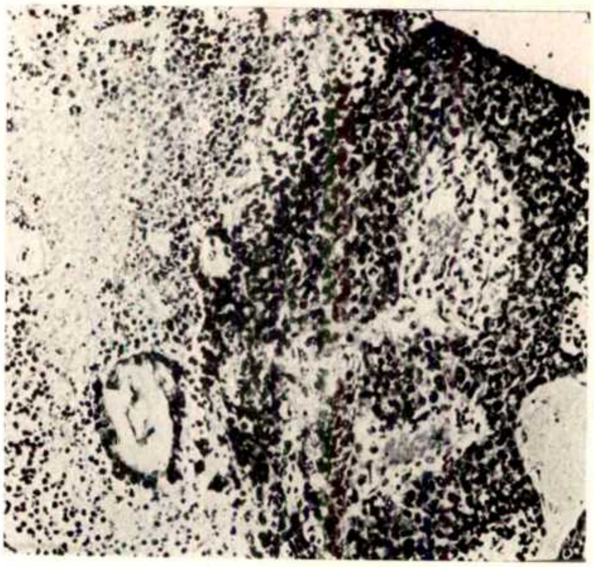


FIG. 6.

Pathology of iris and cornea (A-HX10 and A-HX40) showing an undifferentiated bronchogenic carcinoma involving the iris, the ciliary body, the anterior chamber, cornea and corneal endothelium.

undifferentiated metastatic neoplasm of bronchogenic origin involving the iris and ciliary body (Figs. 4, 5 and 6). The patient died five months later.

DISCUSSION

Ophthalmic metastases usually occur in patients known to have malignant disease elsewhere but may be associated with asymptomatic bronchogenic neoplasms (Radnót 1977).

Most metastatic carcinomas, however, involve the posterior segment of the eye (Duke-Elder, 1966) and rarely the anterior segment (Talegaonkar, 1969).

Treatment in this case consisted of enucleation of the eye because of intractable pain but palliative radiotherapy can often be used with good results. In most cases it would be the treatment of choice (Ferry and Font, 1974).

REFERENCES

BLOCH, R. S. and GARTNER, S., 1971. The incidence of ocular metastatic carcinoma. *Archives of Ophthalmology*, *85*, 673–675.

DUKE-ELDER, W. S., 1966. *System of Ophthalmology*. Vol. 8 (Henry Kimpton, London), pp. 917–919.

FERRY, A. P. and FONT, R. L., 1974. Carcinoma metastatic, study of 227 cases. *Archives of Ophthalmology*, *92*, 276–286.

RADNÓT, M., 1977. Metastatic epibulbar carcinoma. *Ophthalmologica*, *174*, 251–254.

REESE, A. B., 1976. *Tumors of the eye*. 3rd edit. (Harper and Row, Hagerstown, Maryland), pp. 423–460.

TALEGAONKAR, S. K., 1969. Anterior uveal tract metastasis as the presenting feature of bronchial carcinoma. *British Journal of Ophthalmology*, *53*, 123–126.

Books received

We have received the following publication, which has been placed in the Library of THE BRITISH INSTITUTE OF RADIOLOGY for the use of members.

Guidelines for the Use of ILO International Classification of Radiographs of Pneumoconioses. Revised ed., 1980 (ILO Occupational Safety and Health Series 22 (rev.80)). pp.48. ILO, Geneva. ISBN 92-2-102463-6.

This is intended for use with the Classification, a set of 22 standard radiographs providing examples of the various types and stages of the disease, which is available from the ILO London office, 96/98 Marsham Street, London SW1P 4LY at £100 or from Geneva at 400 Swiss francs or US $250, all plus postage and insurance.

1981, *British Journal of Radiology*, *54*, 149–151 FEBRUARY 1981

Short communications

Human whole-body NMR tomographic imaging: normal sections

By *W. A. Edelstein, B.S., Ph.D., †J. M. S. Hutchison, B.Sc., Ph.D., F. W. Smith, M.B., Ch.B., D.M.R.D., F.F.R., J. Mallard, D.Sc., F.Inst. P., F.R.S.E., G. Johnson, B.A., M.Sc. and T. W. Redpath, B.Sc., M.Sc.

Department of Bio-Medical Physics and Bio-Engineering, University of Aberdeen; Aberdeen Royal Infirmary

(*Received July 1980 and in revised form October 1980*)

ABSTRACT

In this paper we demonstrate the kind of images that can be produced by a nuclear magnetic resonance (NMR) tomographic section imager from healthy human subjects. Details of the instrumentation and imaging techniques can be found elsewhere (Hutchison *et al.*, 1980; Edelstein *et al.*, 1980), but a brief description of the imaging method is given here.

Our imaging machine is based on a four-coil, air-cored electromagnet manufactured by the Oxford Instrument Company. It produces a magnetic field of 0.04 T and a consequent NMR frequency of 1.7 MHz for the hydrogen protons of body tissues. Our machine uses the NMR signals from hydrogen protons in water and in fat.

The machine produces two kinds of image. The first uses proton density as the imaging parameter, and the second uses proton spin-lattice relaxation time (T_1). T_1 in wet tissues depends essentially on the relative proportions of free and bound water within the tissue under examination; tissues with more free water have longer relaxation times (Packer, 1977). T_1 values of normal and malignant animal and human tissues have been presented (*e.g.* Damadian *et al.*, 1973; Mallard *et al.*, 1980; Ling *et al.*, 1980) and their implications for *in-vivo* clinical NMR imaging have been discussed (Mallard *et al.*, 1980).

The data for each section (including both proton density and T_1 information) consist of 128 electrical signals, each signal being collected during a one-second interval. Thus the data from an entire section are gathered in just over two minutes. This compares favourably with previous body-section NMR images, such as that demonstrated by Mansfield *et al.*, (1978) which took 40 minutes.

Each electrical signal is a projection (of a thick slice of the body) onto the same single selected axis. The image reconstruction utilizes the phase information contained in the NMR signal as well as its amplitude. This differs from X-ray and radionuclide CT data where only intensity information is available and different projections must be made from different angles.

The technique of projections onto a single axis has the advantage that curvature of the projecting lines should produce only a geometric distortion of the final image and not a degradation of spatial information which could occur if a multiple-angle projection method were used. NMR imaging is particularly subject to such curvature distortion because of possible inhomogeneities in the static, gradient or radio-frequency magnetic fields employed.

Our tomographic sections have a Gaussian profile with thickness (equivalent rectangular width) of 18.5 mm. Each imaging element is 7.5 mm wide × 7.5 mm high × 18.5 mm thick, composing a volume of 1 cm^3. In each imaging element, the uncertainty in proton density for muscle tissue is about 2.5% and the uncertainty in T_1 is about 3.5% for T_1 about 200 ms, with some worsening as T_1 departs from that optimum value.

To evaluate our system we have examined 11 healthy volunteers aged 20 to 55 years. We have obtained tomographic sections from head, thorax and abdomen (including pelvis). No adverse effect was experienced by any of the volunteers either during or after the examination.

RESULTS

In the head most of the important structures have been demonstrated. Figure 1 shows the cerebral cortex, pineal gland, the choroid plexes and the sagittal sinus in a 27-year-old female volunteer. Lower sections have demonstrated the cerebellum, fourth ventricle and brain stem. The paranasal sinuses, orbits, eyes and ocular eye muscles have also been seen.

Sections through the thorax have demonstrated very clearly the major blood vessels, heart and lungs: these are best seen in the T_1 images. The chest wall and breast tissue are best demonstrated in the proton density images. Figure 2 is a section at the level of the fifth dorsal vertebra in a 33-year-old female and shows clearly the right and left ventricles of the heart, the left main pulmonary artery and the descending aorta. The lungs, breast and arms are also clearly seen.

Abdominal sections have again demonstrated the major blood vessels and organs. The liver, spleen and kidneys are especially well seen in the T_1 images. The stomach and colon are seen in both the proton density and T_1 images, especially when a gas/fluid level is present. Figure 3, a section at the level of the twelfth dorsal vertebra and first lumbar vertebra, shows clearly the vertebral canal and lumbar muscles in the proton density image in the same female subject as Fig. 2. The T_1 image shows the liver with the splenic vein draining into the porta hepatis together with the spleen and the upper pole of the left kidney. A fluid level is seen in the stomach. We were not able to demonstrate the pancreas in any of the volunteers. The small bowel is seen as a conglomerate of different densities which is more clearly demonstrated when it is surrounded by fat.

In the pelvis the descending colon, rectum and bladder are easily seen as are the testes in the male.

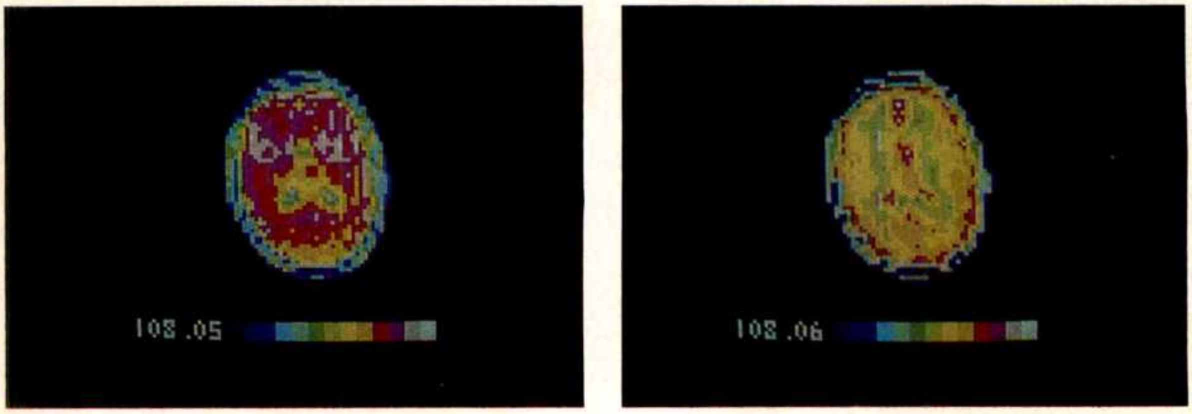
DISCUSSION

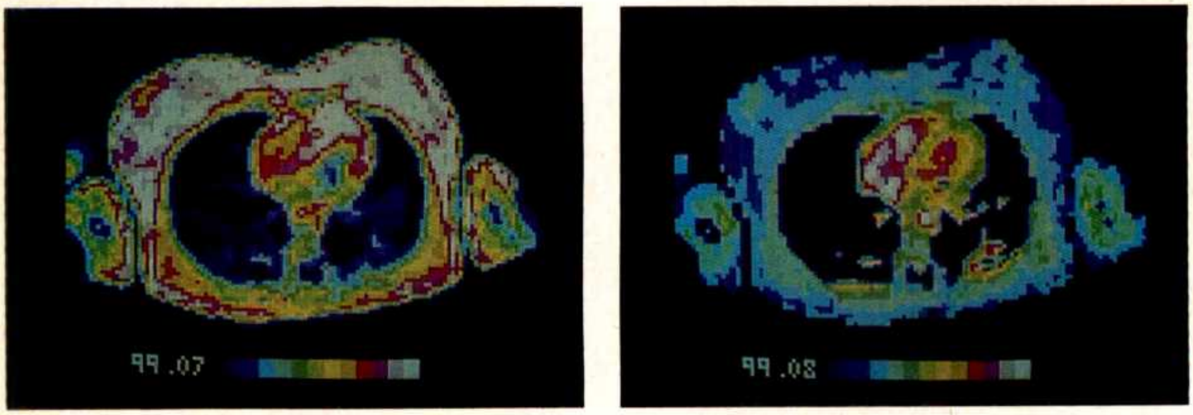
We believe our equipment provides a potentially useful diagnostic imaging system which should provide valuable information in the investigation and diagnosis of a large number of conditions. It does not use ionizing radiation, and there is no evidence of objective or subjective, short or medium term effects arising from the radiofrequency, gradient or static magnetic fields at the levels we employ (NRPB, 1980). It appears, therefore, to be a safe, noninvasive technique. In addition, images are formed of any transverse section across the body which displays either the distribution of protons in water and fat or the spin-lattice relaxation time, T_1, of those protons. Thus two completely new imaging parameters can now be used to characterize normal and diseased tissue for investigation and diagnosis.

---

*Now at General Electric Corporate Research and Development, Schenectady, NY, USA.

†Requests for reprints.





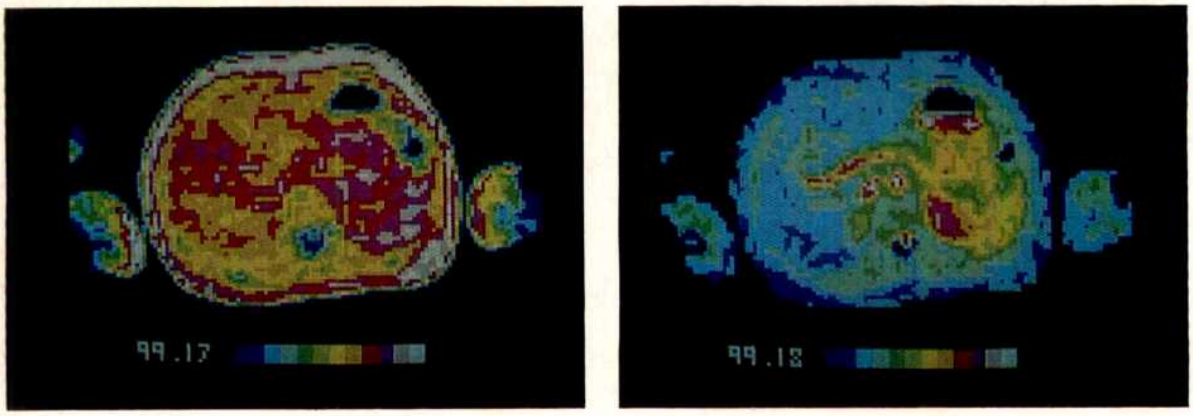
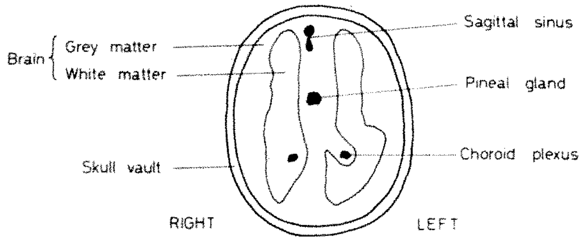


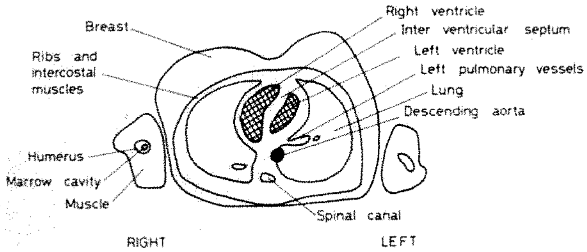
FIG. 1A	B		C
FIG. 2A	B		C
FIG. 3A	B		C

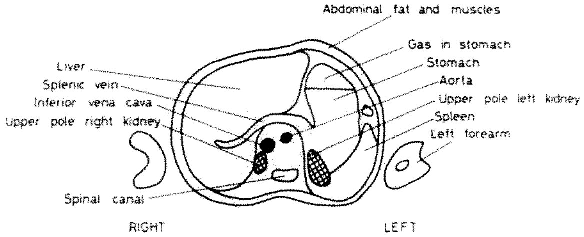
FIG. 1. Axial section of the head at the level of the pineal gland in a 27-year-old female.
(A) proton density; (B) relaxation time, T_1; (C) diagram.

FIG. 2. Axial section through the thorax of a 33-year-old female at the level of the fifth dorsal vertebra.
(A) proton density; (B) relaxation time, T_1; (C) diagram.

FIG. 3. Axial section through the upper abdomen of the same 33-year-old female at the level of the 12th dorsal vertebra.
(A) proton density; (B) relaxation time, T_1; (C) diagram.







This new technique should be useful in the investigation of the head and neck, thorax and abdomen. Its use in the investigation of pelvic disease in both the male and female should be pursued because of the absence of ionizing radiation, and its potential as a breast scanning agent should be explored. Whilst it will be used to provide information on those conditions which can also be studied by other imaging techniques, this new procedure may provide further information not yet readily available. It also seems very likely that it may provide useful clinical information on many conditions which have not, so far, yielded to other imaging techniques, for example inflammatory or oedamatous states.

As a beginning of the exploration of its role, we are presently studying a number of patients who have primary carcinoma plus evidence to suggest the presence of either hepatic or pulmonary metastases.

ACKNOWLEDGMENTS

We are grateful to the Medical Research Council for funding this project and in particular for providing support for W.A.E. G.J. and T.W.R. are in receipt of MRC studentships. We are all indebted to Dr. Anne Reid for her active help, and to all the volunteers in the series. Patents are held on this instrument for the University of Aberdeen and the Medical Research Council by the National Research Development Corporation.

REFERENCES

DAMADIAN, R., ZANER, K., HOR, D., DIMAIO, T., MINKOFF, L. and GOLDSMITH, M., 1973. Nuclear magnetic resonance as a new tool in cancer research: human tumors by NMR. *Annals of the New York Academy of Sciences, 222*, 1048.

EDELSTEIN, W. A., HUTCHISON, J. M. S., JOHNSON, G. and REDPATH, T. W., 1980. Spin warp NMR imaging and applications to human whole-body imaging. *Physics in Medicine and Biology, 25*, 751–756.

HUTCHISON, J. M. S., EDELSTEIN, W. A. and JOHNSON, G. 1980. A whole-body NMR imaging machine. *Journal of Physics E: Scientific Instruments, 13*, 947–955.

LING, C. R., FOSTER, M. A. and HUTCHISON, J. M. S. 1980. Comparison of NMR water proton T_1 relaxation times of rabbit tissues at 24 MHz and 2.5 MHz. *Physics in Medicine and Biology, 25*, 748–751.

MALLARD, J. R., HUTCHISON, J. M. S., EDELSTEIN, W. A., LING, C. R., FOSTER, M. A. and JOHNSON, G. 1980. *In-vivo* NMR imaging in medicine: the Aberdeen approach, both physical and biological. *Philosophical Transactions of the Royal Society, B, 289*, 519–530.

MANSFIELD, P., PYKETT, I. L., MORRIS, P. G. and COUPLAND, R. E. 1978. Whole-body line-scan imaging by NMR. *British Journal of Radiology, 51*, 921–922.

NRPB 1980. Outline of advice on exposure to nuclear magnetic resonance clinical imaging. *NMR* 2/80/3. (in press).

PACKER, K. J. 1977. The dynamics of water in heterogeneous systems. *Philosophical Transactions of the Royal Society, B, 278*, 59–87.

1981, *British Journal of Radiology*, *54*, 152–154

Whole-body tomographic imaging by NMR*

By V. Bangert and P. Mansfield

Department of Physics, University of Nottingham

and R. E. Coupland

Department of Human Morphology, Queen's Medical Centre, University of Nottingham

(*Received August 1980 and in revised form September 1980*)

Since producing our first whole-body nuclear magnetic resonance (NMR) line-scan images some two years ago (Mansfield *et al.*, 1978), we have made a number of changes to our imaging machine which have made possible a considerable improvement in picture quality together with a substantial reduction in imaging time. Other approaches to NMR imaging are extensively discussed and reviewed elsewhere (Mansfield, 1976; Brunner and Ernst, 1979; Mansfield and Morris, 1981).

The present technique utilizes a selective radio-frequency pulse and switched magnetic field selection gradient (Mansfield *et al.*, 1976) used initially to define a thin slice through the specimen. The excited plane of nuclear spins arising from the distribution of protons in the tissues produces a transient signal in a second "read" gradient. This signal is Fourier transformed to give the projection of the total spin distribution in a direction orthogonal to the read gradient. Successive projections produced by mechanically rotating the read gradient are subsequently formed into a two-dimensional picture array using a filtered back projection algorithm (Brooks and di Chiro, 1976). This technique is the NMR analogue of the successful X-ray tomographic technique developed by Hounsfield (1973). In the present images, the slice thickness was set to a nominal 2.0 cm, but it can be varied as required. The imaging time was 9.5 minutes with a pulse repetition period of 0.32 seconds and an average of 16 shots per projection. The NMR operating frequency was 4.0 MHz corresponding to a static magnetic field of 950 G.

The patient is introduced along the magnet axis on a guided non-metallic bed fitted with rollers. Full experimental details, including the RF transmitter and receiver coil arrangement, will be given elsewhere.

Several cross-sectional images through a live subject (VB) were made with the imaging machine some seven hours after eating, following a setting-up and calibration procedure using a phantom comprising 103 water-filled test-tubes arranged in a rectangular array. The subject was lying in a supine position.

The whole-body image shown in Fig. 1 is a transverse section through the abdomen at the level of the disc between the first and second lumbar vertebra (L1–2). Figure 2 is a line tracing of Fig. 1 labelling the recognizable morphological detail. In these images, bright zones correspond to large signals arising from the mobile protons in the water and fat distributed among the various tissues and organs. Dark regions correspond to absence of mobile protons, as expected for example in bone and in gas-filled cavities.

In addition to the clear body outline, Fig. 1 shows ten ribs (R) more or less symmetrically disposed about the midline, as expected. Also clearly visible is the vertebral column (V) with part of the intervertebral disc indicating L1–2, and posterior to this, parts of the neural arch containing the spinal cord. Of particular interest is the aorta (a), shown as a dark circular region anterior to the vertebra, while lateral to this on the right side of the body is the larger dark circular profile of the vena cava. Both vessels are outlined by tissue which gives a strong signal and represents areolar tissue and pancreas (P). In the anterior part of this bright zone lie two smaller circular dark shadows, the superior mesenteric artery (sa) and vein (sv).

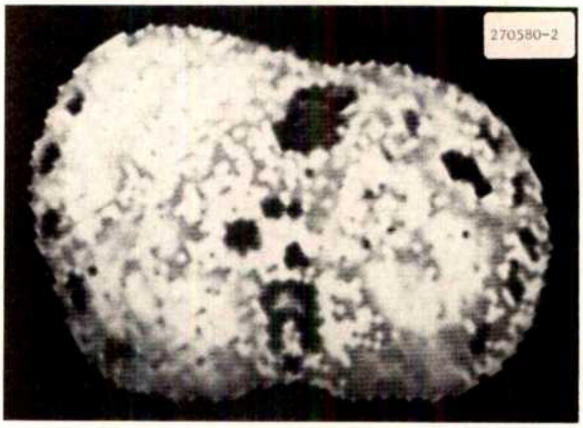


FIG. 1.

Sectional NMR image through the abdomen at L1–2. The right side of the subject lies to the left of the picture and the back is inferior. Bright zones correspond in general to high mobile-proton content (*e.g.* water and fat). See Fig. 2 for structural details.

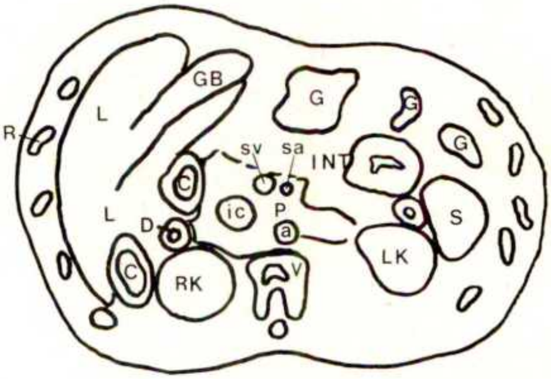


FIG. 2.

Line tracing of Fig. 1. C = colon, D = duodenum, G = gas in stomach, GB = gall bladder, INT = intestines, RK and LK = right and left kidneys, P = pancreas, R = rib, S = spleen. a = aorta, ic = inferior vena cava, sa = superior mesenteric artery, sv = superior mesenteric vein, L = liver, V = vertebra.

---

*Please address all correspondence and reprint requests to Professor P. Mansfield, Department of Physics, University of Nottingham, Nottingham NG7 2RD.

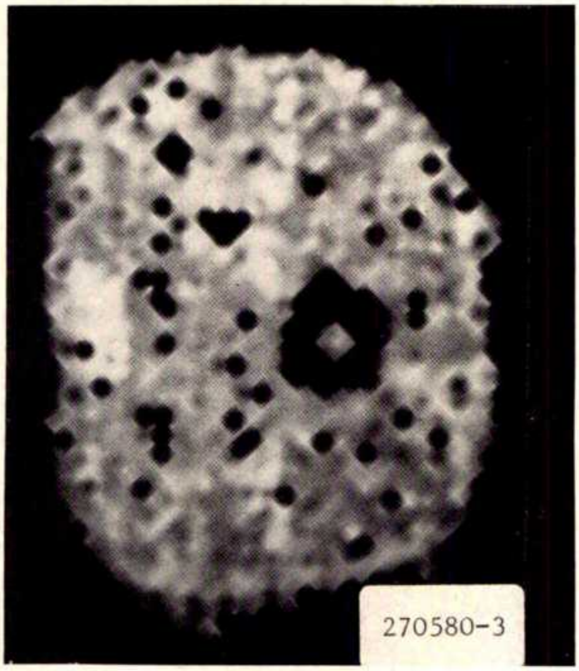


FIG. 3A.

Sectional image through the junction of upper $\frac{1}{3}$ and lower $\frac{2}{3}$ of left thigh. The femur is clearly visible together with muscle groups evident by a medium-intensity signal surrounded by high-intensity signals of areolar and adipose tissue. As in Fig. 1 major blood vessels give no signal and appear dark. See Fig. 3B for structural details.

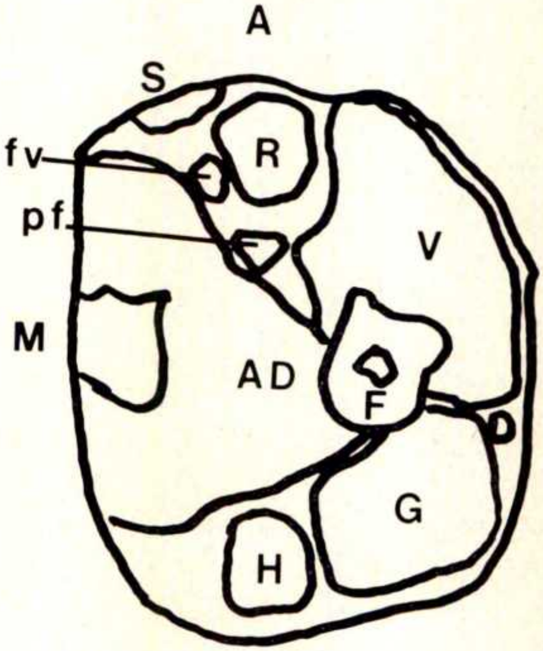


FIG. 3B.

3B Line tracing of Fig. 3A. A = anterior aspect, M = medial aspect of thigh, AD = adductor muscles, F = femur, G = gluteus maximum, H = hamstrings, R = rectus femoris, S = sartorius, V = vasti, fv = femoral vessels, pf = profunda femoris vessels.

The bright zone to the right of the vertebra is the right kidney (RK). The bright mass to the right and anterior to the kidney is the liver, and the gall bladder (GB) which gives a strong signal can be defined. Surrounding the vertebra are the psoas muscles and to the left the left kidney (LK) and spleen (S). The dark irregular cavities lying anteriorly (G) represent gas in the stomach; the oblique sections through the surrounding stomach wall give a moderately intense (bright) signal. Sections through intestine appear as moderately dark peripheral outlines, representing the wall of the gut, with brighter centres (C, D, INT, etc).. Obliquely sectioned portions of the intestines containing fluid are visible anterior and lateral to the pancreas as indicated.

Figure 3A is a cross-sectional image through the junction of the upper and middle one-third of thigh and Fig. 3B is a labelled line tracing. A is anterior, M medial. The femur is clearly visible as a dark ring enclosing the brighter marrow. Some increase in signal (brightness) is apparent around the periphery and is attributed to a thin layer of subcutaneous fat. Muscular groups appear as moderately dark images separated by brighter areas due to the presence of areolar and adipose connective tissue in the latter, confirming the predictions of Pykett and Mansfield (1978). Of particular interest are the well-resolved dark profiles of the femoral vessels (fv) and profunda femoris vessels (pf). Muscles that can be identified include the vasti (V), rectus femoris (R), adductors (AD), sartorius (S), hamstrings (H) and gluteus maximus (G). The sciatic nerve would contribute to the strong signal evident between AD, G and H.

The clear delineation of the blood vessels as dark zones, in spite of the fact that blood is rich in protons, is attributed both to the long spin-lattice relaxation time T_1 of blood and to the rapid movement of the blood through the imaging plane. The same explanation accounts for the darker image of the intestinal wall than of the fluid content at a phase when digestion is occurring. The clarity of the major blood vessels in both the abdomen and limb demonstrated here for the first time is most encouraging and shows that involuntary movements in the supine position present less of a problem than was at first thought. The potentially valuable and interesting study of blood flow in normal and pathological conditions now begins to look much more feasible using this direct but non-invasive technique with suitable modifications and shorter imaging times.

Preliminary experiments with conditions similar to those used here were first performed on the same subject in February 1980. No biomagnetic effects, acute or otherwise, have been experienced.

The static magnetic field strength, the mean absorbed RF power at 4.0 MHz and the field gradient switching rates used in these experiments were all well within the recommended provisional safety limits for NMR imaging as outlined recently by the National Radiological Protection Board's notes for interim guidance (NRPB, 1980).

ACKNOWLEDGMENTS

We wish to thank the Medical Research Council and the Department of Health and Social Security for major grants supporting the whole-body imaging project. We are also grateful to Drs. P. G. Morris and I. L. Pykett and Messrs. R. J. Ordidge and R. R. Rzedzian for their help and advice in many phases of the work. We would also like to acknowledge the help of T. Galton and D. Long of the SRC Appleton Laboratory in producing Figs. 1 and 3 from our data using an Optronix photowriter.

1981, *British Journal of Radiology*, *54*, 154–155

REFERENCES

Brooks, R. A. and di Chiro, G., 1976. Principles of computer assisted tomography (CAT) in radiographic and radioisotopic imaging. *Physics in Medicine and Biology*, *21*, 689–732.

Brunner, P. and Ernst, R. R., 1979. Sensitivity and performance time in NMR imaging. *Journal of Magnetic Resonance*, *33*, 83.

Hounsfield, G. N., 1973. Computerized transverse axial scanning (tomography). *British Journal of Radiology*, *46*, 1016–1022.

Mansfield, P., 1976. Proton spin imaging by nuclear magnetic resonance. *Contemporary Physics*, *17*, 553–576.

Mansfield, P., Maudsley, A. A. and Baines, T., 1976, Fast scan proton density imaging by NMR. *Journal of Physics*, *E*, *9*, 271–278.

Mansfield, P. and Morris, P. G., 1981. NMR imaging in medicine and biology. Special supp. to *Advances in Magnetic Resonance* ed. J. S. Waugh (Academic Press, New York).

Mansfield, P., Pykett, I. L., Morris, P. G. and Coupland R. E., 1978. Human whole-body line-scan imaging by NMR. *British Journal of Radiology*, *51*, 921–922.

NRPB *ad hoc* Advisory Committee on NMR Imaging, 1980. Exposure to nuclear magnetic resonance clinical imaging. *Lancet*, *ii*, 103.

Pykett, I. L. and Mansfield, P., 1978. A line scan image study of a tumourous rat leg by NMR. *Physics in Medicine and Biology*, *23*, 961–967.

Teratogenic and radiosensitizing effects of misonidazole on mouse embryos

By C. Michel and *Hedi Fritz-Niggli

Radiobiological Institute, University of Zürich, CH-8029 Zürich, Switzerland

(*Received July 1980 and in revised form August 1980*)

Teratogenesis, mutagenesis and carcinogenesis are among the most notable radiation effects in man. There is a continued need to find correlation between these biological responses and also to assess the effects or risks of the combined action of radiation and chemicals. Using the embryonic development of mice as a test system we are investigating the efficacy of low-dose irradiation and the possible influence of drugs on radiation-induced developmental anomalies (Michel and Fritz-Niggli, 1978). Embryonic cells and tissues are known to be particularly sensitive to radiation, drugs and stress and show some similarities to tumour cells with regard to metabolic functions such as cell proliferation, energy production and immunological response. Therefore data from the modification of radiation effects by drugs or chemicals in this experimental system may also be of practical relevance in the field of radiosensitization in radiotherapy. Moreover these data are important for risk estimations and radiological protection of the human embryo and fetus.

The radiosensitizing ability of misonidazole has been proved in a great number of investigations. Some *in-vivo* studies with this 2-nitroimidazole have also revealed toxic effects of the drug, depending on the total dose given (Schärer, 1972; Johnson *et al.*, 1976; Dische *et al.*, 1978; Conroy *et al.*, 1979). Both misonidazole and metronidazole, a 5-nitroimidazole derivate, have shown mutagenic effects (Mitelman *et al.*, 1976; Rupp *et al.*, 1978; Chin *et al.*, 1978). Insufficient data are available regarding the teratogenicity of these two drugs. But in the case of metronidazole the drug is classified as possibly having a teratogenic effect in humans and therefore should be avoided in pregnancy (Golbus, 1980).

The object of this study was to gain information concerning the teratogenic activity of misonidazole and its influence on the frequency of radiation damage in mouse embryos. Misonidazole (donated by Hoffmann-LaRoche & Co. Basel) was injected intraperitoneally in pregnant NMRI mice on day eight of gestation. For a teratological study three different drug concentrations were used (200, 670 and 1000 mg/kg) and a dose of 670 mg/kg was applied in an experiment on radiomodification. In both investigations the endpoints studied were embryonic and fetal death, malformation and growth retardation determined on day 13 or 18. Growth retardation was established if the fetal weight was two standard deviations below the average of control values. X-irradiation (140 kV) and 15 MeV electrons were given without anaesthesia with a single dose of 0.01 Gy (1.0 rad).

The administration of 1000 mg/kg misonidazole alone resulted in short-term toxic symptoms such as convulsions, but no lethality of female animals occurred between day eight and day 13. The drug was significantly toxic to the embryo with 670 and 1000 mg/kg (Fig. 1). With the lowest

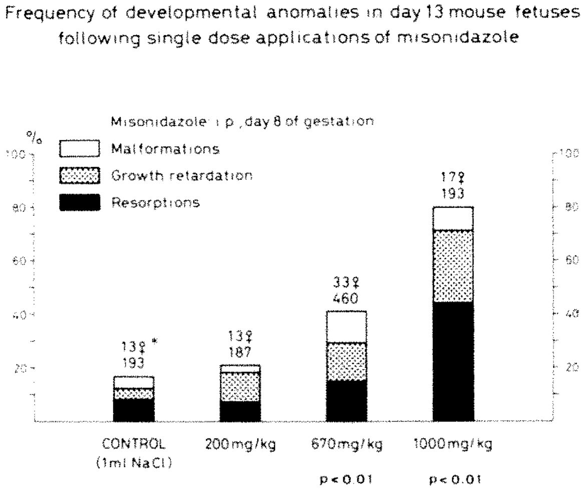


Fig. 1.

Frequency of developmental anomalies in 13 day mouse fetuses following single-dose applications of misonidazole. upper number: females investigated; lower number: implants.

---

*Supported by the Swiss National Foundation for Scientific Research.

TABLE I

INCIDENCE OF RESORBED, DEAD AND ABNORMAL FETUSES ON DAY 18 OF GESTATION. WHOLE-BODY IRRADIATION WITH 0.01 Gy (1 RAD) ON DAY EIGHT. MISONIDAZOLE (670 mg/kg) INJECTED IP 30 MIN BEFORE IRRADIATION

Treatment	No. females	Total implants	No. resorbed and dead fetuses	No. living fetuses: Growth retardation	No. living fetuses: Malformations*	No. living fetuses: Normal fetuses†
Untreated control	28	374	28 (7.5%)	4 (1.2%)	7 (2.0%)	335 (96.8%)
Misonidazole alone	23	302	52 (17.2%)	11 (4.4%)	43 (17.2%)	196‡ (78.4%)
0.01 Gy 140 kV X rays	14	212	19 (9.0%)	6 (3.1%)	9 (4.7%)	178 (92.2%)
Miso + 0.01 Gy X rays	18	234	106§ (45.3%)	7 (5.5%)	49 (38.3%)	72§ (56.3%)
0.01 Gy 15 MeV electrons	15	220	40 (18.2%)	2 (1.1%)	10 (5.6%)	168 (93.3%)
Miso + 0.01 Gy electrons	12	167	43 (25.8%)	10 (8.1%)	38 (30.7%)	76§ (61.3%)

*Cleft palate, hypognathism, exencephaly, eye anomalies, polydactylia.
†Percentage related to living fetuses
‡$p < 0.01$ compared to control (Wilcoxon test)
§$p < 0.01$ compared to irradiation alone

dose (200 mg/kg) the incidence of growth retardation was increased slightly compared to the control, but the difference is not significant ($p > 0.05$, Mann-Whitney-U statistics).

The effects observed on day 18, after single doses of radiation with and without misonidazole (670 mg/kg, 30 min before irradiation on day eight), are shown in Table I. The drug alone considerably reduced the number of normal fetuses, the difference from the control being statistically significant ($p < 0.01$). Irradiation with 0.01 Gy resulted in an insignificant decrease in the frequency of normal fetuses examined on day 18. This finding is in contrast to our earlier data obtained on day 13, where a higher response with the same radiation dose was evident (Michel and Fritz-Niggli, 1978). This discrepancy is due to the lower frequency of growth retardation at term (3.11%) compared to 17.27% on day 13. Irradiation with 15 MeV electrons produced a marked increase of the resorption rate, whereas the frequency of abnormal fetuses remained at the same level as in the X-irradiated group.

Concerning the combined action of misonidazole and radiation on embryonic development, at least an additive mechanism can be observed with electrons. It is interesting to note that in combination with X rays the overall rate of fetal damage is even more pronounced, revealing a synergistic interaction of the two agents. In qualitative respects, the most severely damaged fetuses and the highest incidence of multiple defects were also found in this group.

The present results demonstrate that potentiation of lethal and teratogenic effects can be caused by low-dose irradiation combined with a hypoxic-cell sensitizer. Whether or not the embryonic cells *in utero* can be regarded as being hypoxic during the time of treatment is not known. However, it is quite possible that the specific energy metabolism in embryonic cells, namely glycolytic ATP-formation, may be one of the targets for the radiosensitizing action of misonidazole. We presume that the different degree of radiosensitization between X rays and electrons depends on dissimilar vulnerability of repair systems due to small variations in radiation quality.

REFERENCES

CHIN, J. B., SHEININ, D. M. K. and RAUTH, A. M., 1978. Screening for the mutagenicity of nitro-group containing hypoxic cell radiosensitizers using Salmonella typhimurium strains TA 100 and TA 98. *Mutation Research, 58*, 1–10.

CONROY, P. J., VON BURG, R., PASSALACQUA, W., PENNEY, D. P. and SUTHERLAND, R. M., 1979. Misonidazole neurotoxicity in the mouse: Evaluation of functional, pharmacokinetic, electrophysiologic and morphologic parameters. *International Journal of Radiation Oncology, Biology and Physics, 5*, 983–991.

DISCHE, S., SAUNDERS, M. I., ANDERSON, P., URTASUN, R. C. KÄRCHER, K. H., KOGELNIK, H. D., BLEEHEN, N., PHILLIPS, T. L. and WASSERMAN, T. H., 1978. The neurotoxicity of misonidazole. The pooling of data from five centres. *British Journal of Radiology, 51*, 1023–1024.

GOLBUS, M. S., 1980. Teratology for the obstetrician: Current status. *Obstetrics and Gynecology, 55*, 269–277.

JOHNSON, R., GOMER, C., AMBRUS, J., PEARCE, J., and BOYLE, D., 1976. An investigation of the pharmacological and radiosensitizing effects of the 2-nitroimidazole Ro-07-0582 in primates. *British Journal of Radiology, 49*, 294–295.

MICHEL, C. and FRITZ-NIGGLI, H., 1978. Radiation-induced developmental anomalies in mammalian embryos by low doses and interaction with drugs, stress and genetic factors. In *Late Biological Effects of Ionizing Radiation*, Vol. II (IAEA, Vienna), pp. 397–408.

MICHEL, C., FRITZ-NIGGLI, H., BLATTMANN, H. and CORDT-RIEHLE, I., 1977. Effects of low-dose irradiation with X rays and pi-mesons on embryos of two different mouse strains. *Strahlentherapie, 153*, 674–681.

MITELMAN, F., HARTLEY-ASP, B. and URSING, B., 1976. Chromosome aberrations and metronidazole. *Lancet, ii*, 802.

RUPP, W. D., MROCZKOWSKI, Z., and AGRAWAL, K. C., 1978. Hypoxic radiosensitizers: prospects for effective compounds with fewer toxic side-effects. *British Journal of Cancer, 37*, 60–63.

SCHÄRER, K., 1972. Selektive Purkinje-Zellschädigungen nach oraler Verabreichung grosser Dosen von Nitroimidazol-Derivaten am Hund. *Verhandlungen der Deutschen Gesellschaft für Pathologie, 56*, 407–410.

1981, *British Journal of Radiology*, *54*, 156–157

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Neurotoxicity with desmethylmisonidazole

THE EDITOR—SIR,

There are now underway many clinical trials of misonidazole as an hypoxic cell sensitizer in radiotherapy. Because of the risk of neurotoxicity the total dose which may be given has been limited and in most trials a total of 12 g per square metre of surface area is set as the maximum. This limitation has given further stimulus to the search for drugs which may have a better therapeutic ratio. A direct correlation has been found between the tissue exposure to misonidazole as indicated by the area under the curve of plasma concentration with time and the incidence of neurotoxicity (Dische *et al.*, 1979). Much attention has been concentrated on those nitroimidazoles which have a lower lipophilicity than misonidazole, for in animal studies these drugs show shorter half-lives in plasma and lower concentrations in the central nervous system whilst similar concentrations are detected in tumours (Brown and Workman, 1980).

We have shown that one drug in this group, desmethylmisonidazole, is well absorbed when administered orally to humans (Dische *et al.*, 1980). Desmethylmisonidazole has a partition coefficient (octanol/water) of 0.11 compared with 0.43 for misonidazole. The area under the curve of plasma concentration with time is reduced to nearly half of that with misonidazole and the area under the curve of cerebro-spinal fluid concentration to one-third. The concentrations in human tumours, on the other hand, closely approach those found with misonidazole (Dische *et al.*, 1981). These promising observations have justified the administration of the drug in multiple doses to humans with the prediction that there would be a lower incidence of neuropathy than with misonidazole.

Following satisfactory administration of desmethylmisonidazole in single doses without any observed toxic effects, and after consideration of the laboratory evidence suggesting reduced neurotoxicity with desmethylmisonidazole compared with misonidazole, we decided to administer the drug in multiple doses to 15 patients using the maximum dose now generally applied for misonidazole, 12 g per square metre of surface area. Two of these patients failed to receive the full dose because of reasons not associated with the administration of drug. Of the remaining 13, seven received the drug with radiotherapy on six occasions over a period of three weeks and six were given it daily on 25 to 30 occasions over five to six weeks. These schemes fit regimes of radiotherapy which we employ for patients with advanced (T_4) primary or locally recurrent tumours.

The desmethylmisonidazole was kindly supplied by the Roche Company. The drug has a high solubility and was given orally, dissolved in 10 ml of water, 60 to 90 minutes before radiotherapy.

In five of the 13 patients symptoms of peripheral neuropathy developed and in three there were confirmatory physical signs (Dische *et al.*, 1977). Two of the patients were studied by electromyography which confirmed the presence of a mild sensory peripheral neuropathy. The onset of symptoms was between 25 and 38 days after the beginning of the course of radiotherapy with desmethylmisonidazole. In one case the neuropathy developed before the completion of radiotherapy with desmethylmisonidazole, while in the remainder it appeared between three and 12 days after it was concluded. Symptoms were of moderate severity in three cases and mild in the remaining two. In the three months which have followed, improvement is occurring in all cases and in one the condition has entirely resolved. The symptoms, signs and time-relationship to onset of the peripheral neuropathy were similar to those observed with misonidazole.

A similar incidence of neurotoxicity with both drugs is out of accord with what is to be expected from most of the laboratory studies (Dische *et al.*, 1980). If the area under the curve of plasma concentration with time gives an indication of tissue exposure, then desmethylmisonidazole would seem to be approximately twice as potent in the production of neurotoxicity as misonidazole. Although passage into the cerebrospinal fluid reduces the exposure of the central nervous system more than that of other tissues this may not be relevant to the problem of a peripheral neuropathy. Further, in a dynamic situation lipophilicity may be just one of several factors such as absolute solubility which may be involved in the induction of peripheral neuropathy.

This finding of an incidence of peripheral neuropathy similar to that encountered with misonidazole reduces the possibility that desmethylmisonidazole may give improved radiosensitization in radiotherapy. However, in addition to close observation of the patients for toxic effects, we have monitored the response of normal tissues and of tumour to radiotherapy.

All normal tissue reactions were comparable with those previously observed for the same regimes of treatment employed without the use of any additional measure. In ten of the 13 patients there was complete relief of symptoms due to the primary or recurrent tumour and also an apparent complete regression of the tumour mass. In one case regression was scored as moderate (> 50% decrease in diameter) and in the remaining two there was only a limited regression. The 13 cases included five grossly advanced primary tumours of the breast and single cases of advanced carcinoma of the oesophagus, bronchus, bladder, uterine cervix and an undifferentiated carcinoma of unknown origin; also included were three cases of recurrent carcinoma of rectum, stomach and uterine cervix. The results observed in these patients were considered better than those normally seen in the management of similar T_4 or recurrent carcinomas with similar radiotherapy without use of a radiosensitizer.

No other toxic manifestation was observed other than peripheral neuropathy in these patients; in view of the unusually good responses observed in the patients' tumours a further series of patients are being treated with a combination of desmethylmisonidazole and radiotherapy. This larger experience will be reported in detail at a later time.

Yours, etc.,

*S. DISCHE,
*M. I. SAUNDERS,
†M. R. L. STRATFORD.

*Marie Curie Research Wing for Oncology,
†Gray Laboratory,
Mount Vernon Hospital,
Northwood,
Middlesex HA6 2RN.

(*Received November 1980*)

REFERENCES

BROWN, J. M. and WORKMAN, P., 1980. Partition coefficient as a guide to the development of radiosensitizers which are less toxic misonidazole. *Radiation Research*, *82*, 171–190.

DISCHE, S., SAUNDERS, M. I., LEE, M. E., ADAMS, G. E. and FLOCKHART, I. R., 1977. Clinical testing of the radiosensitizer Ro 07-0582: experience with multiple doses. *British Journal of Cancer*, *35*, 567–579.

DISCHE, S., SAUNDERS, M. I., FLOCKHART, I. R., LEE, M. E. and ANDERSON, P., 1979. Misonidazole. A drug for trial in radiotherapy and oncology. *International Journal of Radiation Oncology, Biology Physics*, *5*, 851–860.

DISCHE, S., FOWLER, J. F., SAUNDERS, M. I., STRATFORD, M. R. L., ANDERSON, P., MINCHINTON, A. I. and LEE, M. E., 1980. A drug for improved radiosensitization in radiotherapy. *British Journal of Cancer*, *42*, 153–155.

DISCHE, S., SAUNDERS, M. I., RILEY, P. J., HAUCK, J., BENNETT, M. H., STRATFORD, M. R. L. and MINCHINTON, A. I., 1981. The concentration of desmethylmisonidazole in human tumours and in cerebro-spinal fluid. *British Journal of Cancer* (in press).

Contrast media for hysterosalpingography

THE EDITOR—SIR,

We were interested to see in your columns the report of a trial of two high cost contrast media, with the conclusion that both were equally satisfactory (Russell and Maguire, 1979).

This stimulated us to undertake a trial comparing one of these contrast media, meglumine iocarmate, containing 280 mg I_2 per ml. (Dimer X), with an older agent (McNabb, 1959) containing a mixture of sodium and meglumine diatrizoates with 290 mg I_2 per ml. (Urografin). The trial was designed with the help of a statistician so that the contrast medium to be used was selected on a randomized basis by the nurse, neither the gynaecologist nor the radiologist knowing which contrast medium was being used. All examinations were performed by one gynaecologist. The indication for the procedure, volume of contrast medium, presence of spasm or reaction to the contrast medium were recorded at the time of the examination. The patient was asked to comment on any pain felt during and ten minutes after injection. She was also given a questionnaire to record any side effects felt during the seven days after examination.

Complete records were available for 53 patients at the end of the trial. There was no difference in the volumes of contrast medium, nor in the incidence of tubal spasm. There was no statistically significant difference in the number of patients in each group feeling pain, although three patients having moderate and one having severe pain (14%) had Urografin (Table I). Markham *et al.* (1977) found 19% of patients having Dimer X had moderate or severe pain.

From the returned questionnaires we found that 40% of women experienced some pain lasting longer than 24 hours. Common side effects were vaginal bleeding and discharge, backache and difficulty in walking. No major reactions occurred, and there was no significant difference in the incidence of delayed pain in the two groups (Table II).

TABLE I

PAIN FELT TEN MINUTES AFTER INJECTION

Pain	None	Mild	Moderate	Severe	Total
Dimer X	13	11	0	0	24
Urografin	12	13	3	1	29

TABLE II

PAIN FELT AFTER LEAVING HOSPITAL

Pain	None	1 day	2–3 days	4–7 days	Total
Dimer X	11	6	5	2	24
Urografin	12	3	8	6	29

The quality of the radiographic images was assessed by two radiologists on a ten point scale. No difference between the two groups was found.

The cost per examination using 10 ml of contrast medium was £7·32 for Dimer X and £0·39 for Urografin.

We have noted that the technique of instrumentation is responsible for much of the pain or absence of pain felt by the patient during hysterosalpingography, and this factor needs to be allowed for in comparisons of contrast media in this procedure.

The primary considerations in choosing a contrast medium are to ensure that the maximum diagnostic information is obtained with the fewest possible side effects. When there is no difference between two contrast media on these grounds we consider that cost should be a deciding factor. For 300 hysterosalpingograms, which would approximate to the number done in this department in one year, the difference in cost for the two media tested is just over £2000–£2197 compared to £117.

We consider that reports on contrast media should include relative cost as part of the information necessary for readers to decide which one they would prefer to use. We are continuing to use Urografin on the grounds that the films are of good quality, the procedure is rapid, there are few side effects and the cost is acceptable.

Yours, etc.,
N. CAPORN,
S. GILANI,
W. D. JEANS.

Bristol Royal Infirmary,
Bristol BS2 8HW.

(*Received October 1980*)

REFERENCES

MARKHAM, G. C., BOTTOMLEY, J. P. and ANSELL, G., 1977. Dimer X in hysterosalpingography. *British Journal of Radiology*, *50*, 101–104.

MCNABB, R. W., 1959. The technique and use of Urografin as a contrast medium in hysterosalpingography. *Journal of the Faculty of Radiologists*, *10*, 108–110.

RUSSELL, J. G. B. and MAGUIRE, B. G., 1979. Metrizamide in hysterosalpingography. *British Journal of Radiology*, *52*, 421–422.

X-ray tube lifetimes with the Leeds General Infirmary EMI brain scanner

THE EDITOR—SIR,

In a recent article in the Journal, the necessity of minimizing "down-time" during tube replacement on an X-ray CT scanner was emphasized, in view of the substantial capital and operating costs of such equipment (Smith, 1980). By the same token, however, we feel that it is also cost-effective to achieve the maximum lifetime possible from an X-ray tube. Whilst the average lifetime for the operation of a tube on an EMI CT1010 brain scanner would appear to be about 300 hours, a small number of centres have consistently achieved significantly greater lifetimes. This letter briefly discusses some of the possible factors which may account for the enhanced performance at the Leeds General Infirmary. Although our experience relates specifically to a brain scanner, it is felt that the discussion may also be of general relevance to other types of scanner.

In his article, Dr. Smith advocates a direct independent measurement of tube output as being the most sensitive method for anticipating tube failure. However, as at most centres, regular scanning of an homogeneous phantom has been used at Leeds as an indicator of scanner performance. Since installation of the CT1010, a daily test-scan of the EMI "toffee" phantom has always been carried out on completion of the manufacturer's recommended "warm-up" procedure, using factors of 120 kV, 33 mA, 210 mm wedges and anti-clockwise 180° index at normal accuracy and

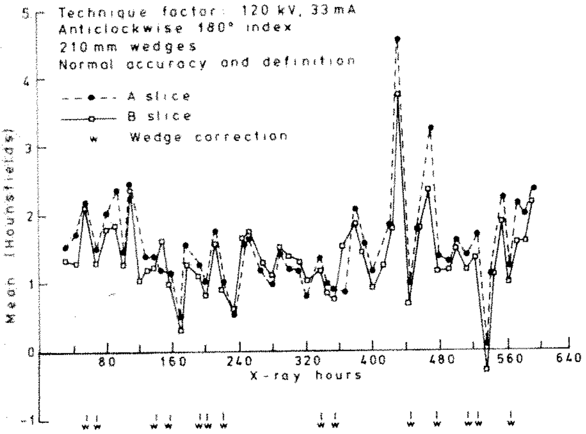


FIG. 1.

Variation of the mean CT numbers observed during a standard test scan on the "toffee" phantom during the entire lifetime of the X-ray tube.

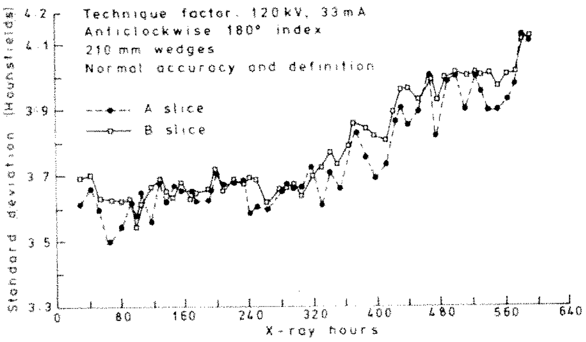


FIG. 2.

Variation of the standard deviations of the mean CT numbers observed during a standard test scan on the "toffee" phantom during the entire lifetime of the X-ray tube.

definition. The results of performing a statistical analysis on the standard circular region of each of the A and B slices of the test-scan are routinely recorded (mean and standard deviation), together with a weekly log of elapsed X-ray hours. Figure 1 shows the mean CT number versus X-ray hours and Fig. 2 the standard deviation versus X-ray hours for both slices, over the complete lifetime of our first tube.

From Fig. 2 it can be seen that after approximately 360 hours, the standard deviations of both slices started to increase and then remained above the limit of 3.7 Hounsfields recommended by EMI for the conditions of the test-scan; tube failure occurred at 596 hours due to a fracture in the poly-carbonate window of the tube shield. For completeness, the oscillations of the means around the assumed "toffee" CT number of 1 Hounsfield are shown in Fig. 1. Similarly shaped graphs were also found for the second scanner tube, which was replaced recently before catastrophic failure after operating for 700 h. Unfortunately, we are unable to say by how much the outputs of the X-ray tubes had fallen by the time they were replaced, or what the 15% decrease in output quoted by Dr. Smith may correspond to in terms of an increase in standard deviation.

Operation of the X-ray tubes beyond the point at which system noise, deduced from the "toffee" scan, is above the limit quoted by EMI, has resulted in a considerable extension of their useful lifetime, some 40% in the case of the tube represented in the Figures and amounting to about six months under the conditions of use at Leeds. During this time no visible loss of picture quality was observed, especially during clinical scans when patient-related artefacts due to poor bolussing etc. are often present in the scans (Shrimpton, 1980). It is therefore felt that continued running of the tubes outside the EMI "factory" tolerance has not unduly compromised the diagnostic capability of the machine, whilst allowing maximum utilization of the tubes.

While the tube lifetimes of 600 and 700 h observed for the Leeds scanner are probably not exceptional, they would appear to be significantly greater than the average figure for CT1010s in the UK, and may have been due to one or more of the following points.

1. The tube cooling system at Leeds has continued to use mineral seal oil instead of other thicker oils recently recommended by EMI. Inspection of our replaced tubes has shown no build-up of residue in the oil ways of the anode block, which might otherwise lead to local overheating.
2. The oil cooler is sited in an outhouse which is ventilated by a forced draught of ambient air. The cooler is also raised above floor level on a 1.5 m high open framework stand, exposing all sides to the air draught.
3. Care is taken to prevent air bubbles from lingering in the tube even when the oil pump is not running. The oil cooler is positioned so that it is always higher than the X-ray tube and the tube is always "parked" and "warmed up" with the tube vertical, cathode at the top.
4. A full-time "warm-up" to 140 kV is always carried out at the start of the working day, and a halftime "warm-up" when X rays have not been used for over 3 h.

A similarly satisfactory tube lifetime was also obtained with the previous Mark I brain scanner at Leeds, which amassed over 1800 X-ray running hours on a single tube without failure before the machine was upgraded to the present CT1010 configuration. The operating conditions were similar to those outlined above.

In conclusion, the operation of the CT1010 brain scanner at the LGI has resulted in satisfactory tube lifetimes, significantly above the apparent national average. We believe that diligence in always observing the correct "warm-up" procedure for both scanners, together with the specific oil cooling system employed, are the major influencing factors in achieving this performance. Maximum utilization of X-ray tubes, without reducing picture quality, must be regarded as being cost-effective.

Yours, etc.
*P. C. SHRIMPTON,
D. W. DEWHIRST.

The University of Leeds,
Dept. Medical Physics,
The General Infirmary,
Leeds LS1 3EX.

(*Received September 1980*)

REFERENCES

SHRIMPTON, P. C., 1980. A shredded-gel bolus material for use with an EMI CT1010 brain scanner, *British Journal of Radiology*, *53*, 148–150.

SMITH, C. B., 1980. Measurement of X-ray tube output in computed tomography: a simple method for anticipating tube failure, *British Journal of Radiology*, *53*, 718–720.

---

*Present address: NRPB, Harwell, Oxon.

1981, *British Journal of Radiology*, *54*, 159–167 FEBRUARY 1981

Proceedings of Symposium Mammographicum 80

Organized in co-operation with The British Institute of Radiology, and held at University College, London, September 5–6, 1980

Session 1. Fundamental aspects of mammography

Chairman: Dr. I. H. Gravelle

Radiologists' requirements, by Dr. A. K. Tucker.
Review of physical factors in mammography, by Dr. D. R. Dance.
Radiographic technique, by Mrs. O. Wilson.
Review of mammographic practice in Britain, by Mr. M. Fitzgerald.

RADIOLOGISTS' REQUIREMENTS

By A. K. Tucker

St. Bartholomew's Hospital, London EC

The radiologist interested in mammography needs to be able to see masses of under 5 mm in the difficult dense breast. The mass must be demonstrated well enough to diagnose its nature, preferably without the intrinsic hazards of ionizing radiation.

The essential basic requirements are high definition, high contrast, and good radiographic technique to include the whole breast. Low dosage techniques are essential.

By reducing the variable contours of the female breast to a homogeneous slab, the definition can be greatly improved, and the radiation dose reduced, especially in film mammography. Compression is therefore one of the most important factors in producing good films.

Film mammography should only be undertaken using a machine built specifically for the purpose. This should have a molybdenum anode and a fine focus, and kilovoltage adjustable from 25–35 kV. It will also have an efficient compression system.

Two important facets of mammography are, firstly, the demonstration of the nature of a known mass, and secondly, the demonstration of the occult tumour, either when a primary cause is sought in known metastatic disease, or as part of a screening service.

As the results of treatment of breast cancer have improved so little since the turn of the century, early diagnosis should be further investigated, to assess the possibility of improved prognosis.

Tumours under 5 mm in size are most frequently detected by the presence of microcalcification. This necessitates a recording system capable of resolving less than 0.1 mm. Artefacts in film handling and processing must be avoided. New developments such as the use of mammographic grids should be assessed.

Clinical information both on the present condition and previous surgery is vital for accurate interpretation, and viewing conditions should be good.

The risk benefit ratios must be taken into account, and these are of minimal consequence for the symptomatic patient. With careful use of modern techniques, the risk benefit ratio is also acceptable for the asymptomatic woman.

REVIEW OF PHYSICAL FACTORS IN MAMMOGRAPHY

By D. R. Dance

Physics Department, The Royal Marsden Hospital
Fulham Road, London SW

This review discusses the physical properties of some of the component parts of mammographic systems.

The interaction of X-ray photons with the female breast depends upon photon energy and breast thickness and composition. The relationship of photon transmission and image contrast to these parameters was considered and it was pointed out that the requirements of high contrast and low dose can be in conflict. Breast compression will decrease dose and improve contrast but similar results cannot be achieved by modifying the X-ray spectrum. X-ray tubes with a molybdenum target/filter combination give high contrast and dose whereas tubes with a tungsten target and aluminium filter give lower contrast and dose at the same peak potential.

Four types of image receptor are currently in use, but only two were reviewed. Mammographic film/screen combinations have adequate resolution and low dose. Rare earth and calcium tungstate phosphors can be used and the performances of the two types of screen are quite similar. The images produced are close to being noise limited and it is necessary therefore to decrease quantum mottle by increasing the number of photons detected and decreasing overall sensitivity. Film/screen combinations should be used with a molybdenum target tube but the Xerox image receptor can give good quality images with a heavily filtered tungsten target. This is because of the edge enhancement in the Xerox image. The radiation dose is higher for Xeroradiography but the magnitude of the difference depends upon the actual techniques compared and the dosimetric parameters used. It is important to use an appropriate measure of dose.

Geometric unsharpness can be the greatest source of image blurring. A small focal spot and a large focus skin distance should be used and the receptor should be placed close to the compressed breast.

RADIOGRAPHIC TECHNIQUES

By Olivia M. Wilson

X-ray Department, The Royal Marsden Hospital,
London SW

Patients for mammography may be divided into two categories: the first category consists of asymptomatic patients over the age of 40 attending for routine screening; the second includes patients presenting with symptoms, those with a previous history, those receiving therapy and post-surgical patients.

For patients in the first category the screening view of choice is the supine lateral which fulfils the requirements for an ideal screening test: sensitivity, low dose, reproducibility and economy. The correct technique should show all the breast tissue and include the retro-mammary space and axilla. With good compression and correct exposure there is detail from the skin thickness to the base of the breast.

The second category of patients requires a more definitive test in order not only to show the presence of an abnormality, but also to precisely indicate the position, size and nature of the abnormality. Two views which may be regarded as basic are: the lateral and the cranio-caudal, the former may either be the supine or the erect medio-lateral. A conscious effort is required to ensure that the maximum amount of breast tissue is included in these images while maintaining the nipple in profile wherever possible. These two views often provide sufficient information for diagnosis.

Sometimes further views are indicated to fully visualize large breasts or to give additional information about specific areas. The following supplementary views may be used: the extended cranio-caudal; the oblique; the axilla-erect or supine; the latero-medial.

At the Royal Marsden Hospital the Xerox system is used and the equipment for supine views consists of a non-dedicated set modified with a long rectangular cone, detachable compression moulds and additional 2 mm aluminium filter. The equipment used for the erect views is dedicated to mammography and has a short fixed focal distance, a set of compression cones and an additional 1 mm aluminium filter.

REVIEW OF MAMMOGRAPHIC PRACTICE IN BRITAIN

By M. Fitzgerald

Radiation Physics Department, St. Bartholomew's Hospital London EC

This review was based on provisional results of a recent postal survey and a comparison was made with the results of a previous study during which 60 centres were visited. Both studies demonstrated a wide variation in practice.

There are about 200 NHS and private centres with mammographic facilities, which is a seven-fold increase since 1965. The patient load is about 3500 per week, varying at each centre from < 1 to 200 per week. Of these, about 33% are "well", 17% are "worried-well" and 50% are symptomatic.

The use of purpose-built X-ray sets has increased from ~70% in 1977 to ~80% now and the majority of centres use a mammographic film-screen system, the most popular being Kodak Min-R and Du Pont Lo-Dose. Of the 14% using the Xerox system, only a quarter use the negative mode with its consequent reduction in dose compared with the positive mode.

The previous physical survey included an analysis of the relation between surface absorbed dose and image quality for different imaging systems. The image quality, measured using a semi-quantitative test phantom, was expressed as an image "score". It was found that Xerox (X) produced the highest mean score and that a molybdenum (Mo) target tube delivered three to four times the dose compared to a tungsten (W) tube. With film (F), the molybdenum target tubes gave a far superior image score to tungsten tubes, although the dose was higher. It was suggested that only the Mo–F or W–X combination should be used for asymptomatic patients and the recent survey showed that over 90% of all patients are now examined by one of these methods. Although the W–F combination is still used in over 10% of centres, the corresponding patient load is only 3% of the total.

A call was made for national agreement on the specification and the technique of measurement of dose in mammography.

Session 2. Clinical aspects of mammography

Chairman: Dr. J. L. Price

A surgeon's viewpoint, by Professor M. Baum.
Pathology in relation to mammography, by Dr. R. R. Millis.
Radiological features of benign breast disease, by Dr. D. L. Asbury.
Special procedures in diagnosis, by Dr. I. H. Gravelle.
Critical analysis of radiological signs in malignancy, by Dr. C. A. Parsons.
Pitfalls in mammographic diagnosis, by Dr. J. L. Price.

A SURGEON'S VIEWPOINT

By Michael Baum

Department of Surgery, King's College Hospital, London SE

The role of mammography in the management of patients with breast symptoms varies from centre to centre depending to some extent on the quality of interaction between the surgeon, the radiologist and the pathologist. Improvements of the service can only occur when there is constant feedback between the three specialist groups.

Patients commonly present to the surgical breast clinic with discrete lumps, generalized lumpiness, pain in the breast, nipple discharge, or without symptoms as a result of attending screening clinics. The role of mammography in investigating these various groups of women according to a set protocol will be outlined in the communication. When seen in the context of a breast clinic it can be judged that mammography plays little part in the diagnosis of a discrete breast lump, which should be managed in most cases by attempted aspiration and needle or excision biopsy for solid lumps. Mammography, therefore, has a role in investigating the doubtful lumpy breast, in raising the index of suspicion of a lump that is clinically benign, and in searching for the second cancer either in the ipsi-lateral or contralateral breast, when the women presents with a clinically obvious cancer on one side. In addition, when a woman presents with metastatic disease with an unknown primary, mammography is one of the essential investigations in searching for the occult lesion. Mammography has little role in examining the patient with a nipple discharge, but the occasional difficult case may be helped by duct injection.

When mammography demonstrates an occult primary lesion, either in the "difficult breast" or as a result of screening a symptomless population, then the radiologist and surgeon have to collaborate in order to localize the lesion and send it for specimen radiology to confirm that the suspicious area has been removed, and then the pathologist has to search carefully in the area of the specimen identified by the radiologist. Using the "double-dye" technique developed in Cardiff, 24 mammographically suspicious areas were subjected to histopathology after biopsy. Of these 13 were benign, the majority being sclerosing adenosis. Eleven were cancer, of which four were invasive and the remainder *in situ*.

Finally, from the surgeons' viewpoint, what is the value of mammography in screening for the early diagnosis of carcinoma of the breast? Most authorities would agree that if screening is to be undertaken, then mammography should play its part, but screening programmes to date have raised more questions than they have answered. For example, what is the natural history of the so-called "minimal" breast cancers detected at screening programmes; how in fact should you treat these lesions and what is the physical and psychological morbidity of the increased biopsy rate? What if any is the carcinogenic risk of the radiation to the breast, and how cost-effective is the whole exercise? In the absence of mortality statistics in this country for screened populations, compared with unscreened controls, one may make the generous premise that each additional node-negative case detected is a life saved, with the further premise that non-invasive cancers will inevitably become invasive, again a generous interpretation of the data. Accepting these premises it may be crudely calculated that the cost of every life saved as a result of a screening programme, is of the order of £40000. Without attempting to place a value on a woman's life, there are probably more effective ways of spending this kind of money within a Health Service starved of resources.

PATHOLOGY IN RELATION TO MAMMOGRAPHY

By Rosemary R. Millis

Imperial Cancer Research Fund Breast Cancer Unit
Guy's Hospital, London SE

Specimen radiography is essential in the management of patients undergoing breast biopsies because of abnormal mammographic findings. The specimen radiograph should be compared with the pre-operative mammogram while the patient is still in the operating theatre, to confirm that the suspicious area has been completely removed, and should also be used by the pathologist as a guide to the abnormal area when selecting tissue for histological examination. Extensive histological examination of such biopsy specimens may be necessary before the presence of a carcinoma can be confirmed or excluded. The use of frozen section is not recommended unless there is an obvious gross lesion.

Clinically occult carcinomas detected by mammography are frequently "minimal cancers" (*in situ* carcinomas or invasive tumours 1 cm or less in maximum diameter). There is also a lower incidence of associated axillary lymph node involvement than is found in patients presenting with a palpable lump.

Calcification is important in the mammographic detection of clinically occult carcinomas. *In situ* duct carcinoma and infiltrating duct carcinoma with a large *in situ* component most frequently contain calcification. Calcification in infiltrating tumours is seen more often in those that are well differentiated. It may not be possible to distinguish between the mammographic appearance of calcification associated with benign and malignant mammary lesions. The microscopic appearance of calcification occuring in carcinomas and some benign conditions is also similar.

The diagnosis of clinically occult carcinomas detected by mammography requires close cooperation between surgeon, radiologist and pathologist.

RADIOLOGICAL FEATURES OF BENIGN BREAST DISEASE

By D. L. Asbury

Department of Radiology, Withington Hospital
West Didsbury, Manchester M20 8LR

On a few occasions mammographic appearances allow a confident histological diagnosis, thereby removing the need for further investigation. These conditions include calcified adenomas, duct ectasia with typical calcifications, lipomas, and superficial skin lesions. In all other circumstances additional invasive procedures such as needle aspiration or biopsy remain necessary because radiological features are not sufficiently specific.

This limitation applies equally to localized mass lesions, such as adenomas and cysts, which may be mimicked, especially in post-menopausal patients, by malignant processes, and to poorly localized disease processes. Amongst the latter are included sclerosing adenosis, fat necrosis, and duct ectasia. These conditions may closely resemble carcinoma both clinically and radiologically. Histological assessment is essential. Likewise, no reliable differentiation can be made between benign and malignant patterns of microcalcification. Biopsy, frequently requiring preliminary needle localization, is mandatory.

Wolfe (1976) has described various parenchymal breast patterns. These patterns are defined and illustrated. The low risk group of N1 and P1 patterns occurred in 67% of his population, but only 18% of cancers developed in this majority grouping. The high risk group of P2 and DY patterns comprised only 33% of his population but 82% of cancers developed in this minority. These findings are critically reviewed.

The primary role of mammography remains the detection of pre-clinical cancer. Except in a very few circumstances it is not sufficiently specific to allow recognition of individual benign diseases nor even reliably distinguish them from malignancy.

REFERENCE

Wolfe, J. N., 1976. Breast patterns as an index of risk for developing breast cancer. *American Journal of Roentgenology, 126*, 1130–1139.

SPECIAL PROCEDURES IN DIAGNOSIS

By I. H. Gravelle

University Hospital of Wales, Heath Park, Cardiff

Galactography. The main indication is the investigation of nipple discharge from one lactiferous duct. If discharge is present from several ducts, the duct showing blood staining or different colour of discharge is selected. Injection of 0.5 ml to 2 ml of 25% Hypaque is followed immediately by mammography.

Several kinds of discharge are found, the type not being specific for any one underlying process. Carcinoma and papilloma may give rise to any type of discharge and do not invariably give rise to blood staining. Other causes of discharge are duct ectasia, fibroadenosis with cysts, granuloma, abscess and epithelial hyperplasia.

An intraductal defect can be due to papilloma, inspissated secretion, granuloma or carcinoma. It is not always possible to differentiate these lesions but the investigation indicates the position and extent of the abnormality and should result in a rational approach to management. Occasionally discharge ceases following injection.

Mammary and nipple infections are contraindications. The commonest complication is extravasation of the medium giving pain. Rarely a mastitis due to sensitivity occurs.

Pneumocystography. The examination is usually carried out when a blood-stained aspirate is obtained on cyst aspiration. It may be used therapeutically in recurring breast cysts. The cyst is aspirated completely and the fluid replaced by an equal volume of air. Mammography is then carried out and cytological and bacteriological examinations of the fluid arranged.

Intracystic masses are usually either papillomata or carcinomata. In most cases it is not possible to differentiate these lesions radiologically but the position and extent of the lesion are demonstrated pre-operatively.

Breast or skin infections are contraindications and breast abscess is a possible complication.

CRITICAL ANALYSIS OF RADIOLOGICAL SIGNS IN MALIGNANCY

By C. Parsons

X-ray Department, The Royal Marsden Hospital
Fulham Road, London SW

The mammographic features of 607 patients with histologically proven carcinoma and 539 patients with benign diagnoses were reviewed. Comparison was made with the parenchymal pattern of 719 controls. Two-thirds of the carcinoma patients showed a soft tissue abnormality on the mammogram and 75% of these were well-defined masses. There was no correlation between histological grade and the clarity of tumour boundary. Tumours presenting solely as an ill defined area of increased density accounted for 25% of those missed by observer error.

Ninety-eight per cent of the spiculated masses were malignant, 74% of the lobulated masses and 30% of the predominantly rounded lesions, although in the latter case there was usually an irregularity of part of the outline. Disturbed architecture was seen in only six cases, three of which were malignant.

One-third of the carcinomas showed calcification. Linear and angular calcifications were four times as frequent in malignant disease as in benign. Round calcifications were equally frequent in cancer and benign dysplasia. The number of calcifications had no predictive significance. Most calcifications in cancer and dysplasia were less than 0.5 mm in diameter. Grouping of calcifications was five times more common in malignancy. Ninety per cent of masses containing calcifications were malignant.

Skin changes were virtually confined to the cancer patients with skin or nipple retraction in one in four. Increased vascularity was less frequent but six times more frequent in cancer than in the benign cases. Assessment of axillary lymph node involvement is inaccuarate with 57 true positive reports out of 67 but only 215 true negatives out of 433.

The P2 parenchymal pattern was three times as common in the cancer patients as in controls.

Only 483 of the 607 carcinomas were diagnosable from the mammogram.

PITFALLS IN MAMMOGRAPHIC DIAGNOSIS

By J. L. Price

Royal Surrey County Hospital, Guildford

An analysis of 30 false negative mammogram reports found in a retrospective study of 327 women with operable breast cancer provided a basis for discussing the pitfalls in mammography. Positioning faults contributed to error in four cases where the cancer was not visible on the film and in six cases diffuse poorly differentiated cancers were obscured by dense breast tissue. Observer error occurred in seven patients and in six of these the lesion was visible in retrospect as distortion or as a dense area in a dense breast. One case was attributable to inattention. Misinterpretation in 13 cases resulted from intracystic carcinomas, mucinous carcinomas presenting as cyst clusters, and small rounded homogeneous sharply defined carcinomatous masses misinterpreted as cysts or fibroadenomas. The use of fine needle aspiration with cytology, pneumocystography, ultrasound and diaphanoscopy reduces error rates where a definitive diagnosis cannot be made by mammography or clinical examination.

In clinical practice the use of mammography reduces biopsy rates in benign breast disease but for the unwary, pitfalls may diminish the specificity of mammography. Microcalcification in the absence of other radiological signs only indicates a high risk area and not a certainty of carcinoma; and on occasion microcalcification may be kept under surveillance. Sclerosing adenosis may be indistinguishable from carcinoma but the subcutaneous fat zone over the lesion tends to remain intact and may be widened. Fat necrosis and haematomas can produce masses and architectural distortion and eventually microcalcification or ring calcification. In fat necrosis the subcutaneous fat layer over the mass or distorted tissue is often widened with a band of increased transradiancy and this sign may be useful in the differentiation from carcinomas.

The defining of the types of breast and areas where errors and pitfalls may present offers some guidance to the clinician in the management of breast disease.

Proceedings of Symposium Mammographicum 80

Session 3. Proffered papers

Chairman: Dr. A. K. Tucker

Correlation of risk factors for breast carcinoma from clinical assessment and mammographic pattern in 1,000 cases, by Professor G. H. Whitehouse, Mr. W. D. George, Dr. A. F. Evans and Mr. P. D. Walsh.
Isomat needle localization, by Dr. E. Cummins.
Diaphanography—a comparison with mammography and thermography, by Dr. J. K. Hussey, Dr. A. F. MacDonald, Dr. D. M. Nichols and Dr. J. Whatmough.
Ultrasound in breast disease, by Ms. M. Reilly, Dr. M. Hussey and Dr. J. T. Ennis.
A comparative prospective evaluation of isotopic breast scanning, mammography and immediate cytology in the diagnosis of breast disease, by Mr. R. A. B. Wood, Dr. H. Duguid, Mr. J. Clark, Mr. P. E. Preece, Dr. F. Hutchinson, Dr. M. L. Wisbey, Mr. G. Neill and Professor A. Cuschieri.
Grid technique in mammography, by G. Jost.

CORRELATION OF RISK FACTORS FOR BREAST CARCINOMA FROM CLINICAL ASSESSMENT AND MAMMOGRAPHIC PATTERN IN 1000 CASES

By G. H. Whitehouse, W. D. George, A. F. Evans and P. D. Walsh

University of Liverpool

The study involves women over 35 years of age who attend a mobile unit where a detailed history is taken, followed by clinical examination of the breasts and mammography. Hormonal studies are also carried out.

The aim is to determine whether or not there is a correlation between certain factors which are regarded as putting women at high risk for developing breast carcinoma and, eventually, to determine the possibility of isolating a particularly "high risk" group who would benefit from frequent breast screening. The Wolfe classification of mammographic patterns has been used (Wolfe, 1976), those with N_1 and P_1 being considered at low risk of developing breast cancer and those with P_2 and DY patterns being at high risk.

Five carcinomas, none of which were clinically apparent, were found on mammography. The percentage incidence of the various patterns was: N_1 21.3, P_1 10.3, P_2 20 and DY 48.4. The incidence of DY rapidly fell from 40 years onward, while the other patterns all showed a slight rise. No correlation was found between mammographic pattern and age at menarche, but the incidence of N_1 was higher with an early menopause while P_2 increased with age of menopause and DY remained unaltered. A very high incidence of N_1 type was found in those women whose first child was born before age 20 years with a correspondingly lower incidence of high risk patterns. Nulliparous women had a low incidence of N_1 but more P_2 and DY patterns in comparison. The severity, duration and nature of breast symptoms was quantified as a "breast symptom digest"; the most severe grade corresponding to a low incidence of N_1 and a high incidence of DY in pre-menopausal women. No relationship was found between mammographic pattern and oral contraception. There was no correlation between a family history of breast cancer and the mammographic pattern.

REFERENCE

WOLFE, J. N., 1976. Breast patterns as an index of risk for developing breast cancer. *American Journal of Roentgenology*, *126*, 1130–1139.

ISOMAT NEEDLE LOCALIZATION

By E. Cummins

Frimley Park Hospital, Surrey

A simple technique using a grid and a fine stilette is described for localization of radiologically suspicious breast lesions which are not palpable clinically. The hooked end of the stilette is placed as near the centre of the lesion as possible as a guide for the surgeon.

DIAPHANOGRAPHY—A COMPARISON WITH MAMMOGRAPHY AND THERMOGRAPHY

By J. K. Hussey, A. F. MacDonald, D. M. Nichols and J. Whatmough

Departments of Radiology and Bio-Medical Physics
Aberdeen Royal Infirmary

Transillumination, as a method of breast examination, was developed by Ohlsson (1977) in Sweden. His technique uses a long wave, predominantly red light source with visual inspection of the breast and a shorter flash exposure photographed by infra red film. The technique is based on the relative opacity of malignant cells compared to normal breast cells, suggesting that its accuracy might be less affected by normal dense breast tissue than other techniques.

We have used Ohlsson's apparatus and technique in over 400 patients and have been able to detect fibroadenomas, fibroadenosis, cysts and carcinoma. The positive detection of breast carcinoma so far has been almost as accurate as mammography with each technique missing one lesion detected by the other. This is much more valuable than thermography which was also carried out on all cases. We have not been able to detect micro-calcification or small cysts and we have not examined a sufficient number of small carcinomas to confirm Ohlsson's figures for the detection of early carcinoma.

Problems of photographic exposure and technical difficulties in delay in infra red film processing have led to a trial of infra red sensitive television and video tape recording.

The conclusion so far is that diaphanography is a very useful method of breast examination, much superior to thermography, and should be used as complementary to mammography in referred cases. It would also be very valuable as a breast screening technique, if comparable accuracy is confirmed in small lesions.

REFERENCE

OHLSSON, B. 1977. Diaphanography—a new method for investigation of the breast. (Available from Dr. Ohlsson, Veberöds Läkärmottagning, S-240 14 Veberöd, Sweden).

ULTRASOUND IN BREAST DISEASE

By M. Reilly, M. Hussey and J. T. Ennis

Department of Radiology
Mater Hospital, Dublin 7, Ireland

Xeromammography, routinely used for breast investigation, subjects the patient to high doses of ionizing radiation, which now renders it unsuitable for use in a screening programme. The success of ultrasound in other soft tissue areas has encouraged the study of its potential in breast diagnosis, and results of such work in the Mater Hospital are presented here.

Patients referred for Xeromammography also underwent an ultrasound examination. The ultrasound procedure is described and the ultrasonic appearance of the normal breast is illustrated. Classification of irregularities is by pattern recognition and a number of patterns consistent with various breast disorders are discussed and illustrated. Correlation with Xeromammography is presented for 98 cases.

A study of the effect of refraction on registration indicates that even a small difference between the speeds of propagation of sound in the water bath and breast tissue has a significant effect on resolution. Simple mathematical models of the breast were used and computer programs written to perform the analysis and display results. A summary of these results is presented.

A video interface to the MDS computer in the Radiology Department is currently being built, and this will enable the storage of ultrasound images on disk for later retrieval and analysis. We propose to write a program package for image enhancement and statistical analysis, and are optimistic that we will contribute to diagnostic accuracy.

A COMPARATIVE PROSPECTIVE EVALUATION OF ISOTOPIC BREAST SCANNING, MAMMOGRAPHY AND IMMEDIATE CYTOLOGY IN THE DIAGNOSIS OF BREAST DISEASE

By R. A. B. Wood, H. Duguid, J. Clark, P. E. Preece, F. Hutchinson, M. L. Wisbey, G. Neill and A. Cuschieri

Departments of Surgery and Medical Physics, Ninewells Hospital, Dundee

This paper will describe a prospective study on patients with breast disease in which $^{99}Tc^{m}$ diethylene triamine penta acetic acid (DTPA) scan, mammography and aspiration breast cytology were reported without access to clinical details by three separate observers.

Patients attending a breast clinic with a breast mass had aspiration cytology performed with immediate staining of the material and a report available in four minutes. Patients were sent for standard mammography or xero-mammography (Rank Xerox), if over the age of 30 years. Scintigraphic views of both breasts were obtained at one hour and two hours after intravenous injection of 8.0 mCi of $^{99}Tc^{m}$ DTPA using an Ohio Nuclear Series Gamma Camera and a high resolution parallel hole low energy collimator. X-rays and scans were reported blind as (1) definitely malignant, (2) very probably malignant, (3) probably malignant, (4) probably normal, (5) definitely normal, (6) uninterpretable.

One hundred and five patients (age range 17–85 years) have been considered in the study. Breast cancer was confirmed histologically in 55 patients (42 post-menopausal) and benign breast disease diagnosed in 50 patients (seven patients post-menopausal) confirmed either histologically or by subsequent follow-up. Results have been assessed by predictive values (Vecchio, 1966). The predictive value of a positive test for cytology was 95%, mammography 78% and DTPA scan 77%. Predictive value for mammography and DTPA scan together was 95%. The predictive value for all three tests was 100%. Experience with DTPA scanning has been favourable with an estimated maximum total radiation dose to both breasts of 200 μGy (mrad) and, when used in conjunction with mammography has an overall diagnostic accuracy equal to that of aspiration cytology.

REFERENCE

VECCHIO, T. J., 1966. Predictive value of single diagnostic test in populations. *New England Journal of Medicine, 274,* 1171–1173.

GRID TECHNIQUE IN MAMMOGRAPHY

By G. Jost

Philips Medical Systems, Eindhoven, Holland

Radiobiological considerations demand a reduction of the radiation dose received in mammography. Dose-reducing film-screen combinations can only be used when there is no associated reduction in image quality. Under the usual examination conditions, currently available low-dose mammography systems yield poorer detail than non-screen mammography film. The image quality of such systems can be improved by the magnification technique, increased focus-film-distance and the use of a soft-radiation grid. Whichever technique is chosen, it is always necessary to compromise between acceptable loss of image information and the required dose reduction.

The magnification technique has definite disadvantages with respect to optimization of the conflicting requirements. On the other hand, appropriate use of the grid technique and an increased focus-film-distance can yield an image quality equal to and sometimes superior to that obtained with non-screen film. This paper reports on the experiences with a mammography unit offering a facility for the latter techniques.

Session 4. Physical aspects of mammography

Chairman: Professor R. E. Ellis

Review of physical assessments of image quality, by Dr. B. M. Moores.
Review of the risk of mammography, by Professor R. E. Ellis

REVIEW OF PHYSICAL ASSESSMENTS OF IMAGE QUALITY

By B. M. Moores

Regional Department of Medical Physics
Christie Hospital, Withington, Manchester M20 9BX

Cost, risks and benefits are fundamental considerations in the assessment of any clinical procedure, whether it be a diagnosis or a treatment. These factors have recently received a great deal of attention in mammography due to a consideration of its potential application as a general screening procedure for healthy women.

Image quality is an important component in any assessment of benefit arising from radiological procedures. It is impossible to assess the efficacy of any investigation without some knowledge of quality. Image quality is intimately related to patient dose and this is a direct measure of risk in diagnostic radiology. It is, therefore, extremely important to understand the trade-offs between quality and dose in all radiological investigations, including mammography.

There are essentially three methods of assessing image quality: (*a*) Objective physical measurements; (*b*) Semi-quantitative subjective visual assessment employing simple test phantoms; and (*c*) Quantitative subjective visual assessment employing threshold contrast and/or statistical analysis (ROC).

(*a*) Objective physical measurements can be made of particular parameters, like sharpness, noise and contrast, which are related to image quality. These can be undertaken on individual components in the image forming process or for a given combination of components. Results of these measurements do not describe overall image quality but merely provide information on specific aspects of system performance. They do, however, help to provide the basic framework for our understanding of the interplay of those parameters which contribute to overall image quality.

(*b*) Semi-quantitative subjective assessment involves the use of simple test phantoms containing structural detail which is relevant to the radiological investigation under consideration. These are extremely useful in providing a general appraisal of the overall image quality produced by a set of radiographic conditions. They can be used to check that image quality has not deteriorated over a period of time or as an aid in choosing the radiographic factors which will provide satisfactory image quality.

(*c*) Quantitative subjective assessment is concerned with the location of threshold detectability, the accuracy with which specific image detail can be detected and the way these are related to radiographic conditions. It enables a more detailed investigation into factors affecting image quality since correctly designed experiments enable the discrimination of relatively small changes in image quality. This can be particularly useful when trying to "squeeze" the maximum benefit out of any imaging system. Because threshold detectability will involve both true and false positive detection rates, statistical techniques like receiver operating characteristic (ROC) analysis may have to be applied in this type of assessment.

REVIEW OF THE RISK OF MAMMOGRAPHY

By R. E. Ellis

Department of Medical Physics, University of Leeds

From the surveys reported by Fitzgerald (this proceedings, p.160) the frequency of mammography in the UK has increased sixfold in the last ten years to the current level of 180,000 examinations per year. The majority of these involve either two or three films using a molybdenum tube and a film-screen receptor. Dance's data (this proceedings, p.159) showed a low-dose film-screen examination gave an exposure of 0.6 R at the skin surface and a mean dose of 0.1 cGy (rad) to the breast. Weighting these results with those from Xerox examinations, which are used with a frequency of 14% and give an exposure at the skin surface of 1–1.5 R per film and a mean breast dose of 0.45 cGy per film, a weighted mammogram representative of present practice in the U.K. would give an exposure at the skin surface of 1.8 R and an average dose to the breast of 0.4 cGy.

These doses are below those recommended by Ellis (1972) as an acceptable level. Since that date further studies have shown that at high dose levels the annual risk of the induction by irradiation of breast cancer is higher by a factor of 1½–3 in those under 30–35 years of age compared with those over 35 years. The risk from mammography has been stated by Upton *et al.* (1977) as "the risk is 3.5–7.5 cases per million age 35 years or older per year per rad to both breasts from the tenth year throughout the remainder of life". This assumes that a linear relationship exists between dose and effect, that doses are additive and that a non-threshold model of the dose-effect relationship is used.

Using these premises, in the follow-up of 180,000 people X-rayed over ten years, assuming that they have five examinations with a total breast dose of 2.0 cGy (rad), there would be 25–54 radiation induced cancers. This assumes that all the people are over the age of 35, that they survive for 30 years and that they have no extra risk during the first ten years. If one assumes that there is an annual incidence of 20000 breast cancers in 25 million women in the UK, the radiation induced cancers in the mammographically screened population would be 0.6–1.2% of the normal incidence.

This risk would appear to make mammographic screening as now proposed an acceptable procedure bearing in mind the limitations of the extrapolation from the high dose data.

REFERENCES

BAILAR, J. C., 1978. Radiation hazards of X-ray mammography. In *Late Biological Effects of Ionizing Radiations* (International Atomic Energy Authority, Vienna), pp. 251–261.

BOICE, J. D. and STONE, B. J., 1978. Interaction between radiation and other breast cancer factors. In *Late Biological Effects of Ionizing Radiations* (IAEA, Vienna), pp. 231–249.

ELLIS, R. E., 1972. Breast cancer following irradiation. *British Journal of Radiology*, *45*, 795–796.

UPTON, A. C., BEEBE, G. W., BROWN, J. M., QUIMBY, E. H. and SHELLABARGER, C., 1977. Report of N.C.I. *ad hoc* working group on the risks associated with mammography in mass screening for the detection of breast cancer. *Journal of the National Cancer Institute*, *59*, 481–493.

Scientific exhibition

A quantitative comparison of selected film-screen combinations for mammography, by Dr. A. E. Kirkpatrick and Dr. J. Law.
Mammography in the early detection of breast cancer, by Dr. P. A. Last and Miss A. Fitzpatrick.
Breast tissue phantom images and radiation exposures for different mammographic receptor systems, by Ms. M. E. Masterson, Dr. D. R. White, Dr. R. E. Snyder, Dr. D. W. Miller, Mr. G. R. Hammerstein, Dr. R. L. A. Kirch, Dr. L. N. Rothenberg and Professor J. S. Laughlin.
An atmospheric pressure ionography system for mammography—preliminary clinical experience, by Dr. B. M. Moores, Mr. J. A. Ramsden and Dr. D. L. Asbury.
Mammographic patterns—the Nottingham approach, and some Nottingham findings, by Mr. P. Doyle and Dr. W. J. Roebuck.

A QUANTITATIVE COMPARISON OF SELECTED FILM-SCREEN COMBINATIONS FOR MAMMOGRAPHY

By A. E. Kirkpatrick and J. Law

Royal Infirmary and Western General Hospital Edinburgh

The imaging performance of various mammographic systems was compared using the test object developed and used by the Hospital Physicists Association in their survey of mammographic practice in the U.K. Four currently available film types (Medichrome, Min-R, NMB, CR3) were used with three screens (MR 50, Min-R, CAWO) at each of five hospitals or clinics, together with positive and negative mode xerography. Both kilovoltage and filtration were varied to give a quantitive relation with image quality.

Both authors (radiologist and physicist) read all the films, and their conclusions did not differ. For Medichrome films an orange light variable colour viewing box was used, and the radiologist had many years experience with blue film.

The authors conclude: (*a*) the highest image score was obtained using NMB film with Min-R screens; (*b*) Differences between NMB and Medichrome film, and between MR 50 and Min-R screens, were not large, particularly for a radiologist accustomed to blue films; (*c*) Xerography shows no gain in image score over the better film-screen combinations, either in positive or negative mode. Its value in mammography may need to be reconsidered.

MAMMOGRAPHY IN THE EARLY DETECTION OF BREAST CANCER

By P. A. Last and A. Fitzpatrick

BUPA Medical Centre, London

Five case reports were illustrated with histories, mammographic findings and follow-up reports.

Case 1 Two specks of microcalcification in 1978 had developed by 1979 into a suspicious cluster of microcalcification. This lesion was a well-differentiated intra-duct carcinoma.

Case 2 A clinically suspicious mass which had previously been ignored was shown by mammography to be malignant. This was subsequently proven on histology.

Case 3 A clinically negative breast examination but with an abnormality suspected by the patient, showed an obvious lesion on mammography.

Case 4 A clinical and symptomatic problem of the right breast—a small cyst, presented on mammography with a unsuspected carcinoma in the opposite breast.

Case 5 A clinically negative breast examination with spiculate microcalcification on mammography. The area was excised without X-ray control or follow-up and two years later a repeat X-ray at the Screening Centre showed widespread recurrence. This was a localized intra-duct carcinoma. This case also demonstrated artefacts due to using a wet supporting sponge.

The present screening procedure is:

Women aged 35 years and over. Two mammographic views—a craniocaudad and a lateral oblique—are taken at the initial visit; thereafter, an annual lateral oblique view only is taken.

Women aged less than 35 years. Mammography is only undertaken if indicated by present findings, previous breast surgery, or a strong family history.

Technique. Screening mammography at present is undertaken using a Siemens Mamomat with an Iontomat attachment, with Kodak NMB film and Kodak Min-R cassettes. The surface-absorbed dose with this technique is 0.2 cGy (rad) per film.

BREAST TISSUE PHANTOM IMAGES AND RADIATION EXPOSURES FOR DIFFERENT MAMMOGRAPHIC RECEPTOR SYSTEMS

By Mary E. Masterson, D. R. White, Ruth E. Snyder, D. W. Miller, G. R. Hammerstein, Roberta L. A. Kirch, L. N. Rothenberg and J. S. Laughlin

Memorial Sloan-Kettering Center, New York

The exhibit showed breast tissue phantom images and corresponding surface radiation exposures for a variety of receptors and radiographic techniques which have been or are now employed in the U.S. For a given receptor system, target-filter combination, and half-value layer, the X-ray and processor conditions were adjusted to achieve "optimized" images as judged by two mammographic radiologists (RES and RLAK). From the measured surface exposure and half-value layer the absorbed dose at 3 cm depth was calculated following the method described by Hammerstein *et al.* (1979).

REFERENCE

HAMMERSTEIN, G. R., MILLER, D. W., WHITE, D. R., MASTERSON, M. E., WOODWARD, H. Q., and LAUGHLIN, J. S., 1979. Absorbed dose in mammography. *Radiology, 130*, 485–491.

AN ATMOSPHERIC PRESSURE IONOGRAPHY SYSTEM FOR MAMMOGRAPHY

By B. M. Moores, J. A. Ramsden and D. L. Asbury

Christie Hospital and Withington Hospital, Manchester

Ionography is a possible replacement for silver halide based imaging systems in diagnostic radiology, which offers greater flexibility in the way the final image is produced and displayed.

The physical design properties which can affect sensitivity and image quality of an ionography system have been studied previously. Based upon these requirements an atmospheric pressure ionography system has been constructed, primarily for use in mammography. An atmospheric gas pressure system was chosen in order to simplify its design and operation. This necessitated the use of a deep chamber to provide adequate X-ray absorption and hence sensitivity. Freon 13B1 gas was chosen as the X-ray absorbing medium because it contains a relatively high atomic number atom (Bromine $Z=35$) and also has a high density. It is a relatively cheap gas, has a high breakdown potential and has satisfactory resolving capability when employed at atmospheric pressure with low X-ray beam energies. The use of a deep chamber requires relatively high charge collecting fields across the chamber (10kV/cm). Spherical plate geometry must also be employed with the facility to accurately align the chamber to the X-ray focal spot. The imaging system is capable of resolving 10 lp/mm and can produce satisfactory images at lower exposures than conventional mammographic film/screen combinations.

The system has undergone clinical trials on 50 symptomatic patients in which the medio-lateral view of the appropriate breast was imaged. Patient handling and positioning with the ionography system was as easy as for a conventional investigation. The mammo-ionograms were developed by means of the powder cloud technique and could be viewed almost immediately.

This investigation has demonstrated that good quality mammoionographic images can be produced easily and at reasonable cost, but there is scope for further development of the method of reading and displaying the latent electrostatic image. One possibility is the use of electronic scanning of the latent electrostatic image together with digital display of the final image.

MAMMOGRAPHIC PATTERNS—THE NOTTINGHAM APPROACH AND SOME NOTTINGHAM FINDINGS

By E. J. Roebuck and P. Doyle

University Hospital, Nottingham

Localized pathology is visualized mammographically as a lesion and/or a reaction superimposed upon a background. It was proposed that mentally to define the background makes superimposed abnormalities more obvious. The background is comprised of three main elements which should be identified in each case: (i) Astley Cooper's ligaments, vessels and fat; (ii) Glandular tissue; and (iii) Generalized conditions such as dysplasia.

The histological features of "Dysplasia" (D) and "Prominent Duct" (P) shadowing were enumerated. It was stressed that the radiological appearance of each type of change may present with variation in three parameters depending on the degree of activity, the extent and the severity of affection in a particular individual at a particular time.

Since the traditional (Wolfe) method of classification is based on the severity of dysplastic appearance (D shadowing) and the extent of prominent duct (P shadowing), it was considered important that any other classification shall be able to be related to this. The Nottingham system of classification was then described and its relationship to the Wolfe classification illustrated; the only differences being the identification of glandular shadowing, and the inclusion of less severe degrees of affection by dysplasia in the Nottingham classification.

The incidence of the various parenchymal patterns in a group of 162 cancer patients and a matched control group of 385 asymptomatic individuals was demonstrated, together with the variation in incidence of the patterns in the two groups analysed by age. The oestrogen receptor status of tumours from the cancer group had been assessed showing a 70% incidence of E.R. positive tumours in individuals with "D" shadowing compared with 50% of patients with "P" shadowing and 24% of individuals classified "Nl". These findings were irrespective of the severity of "D" shadowing or the extent of the "P" shadowing. It was concluded that in the Nottingham population there is an increase of "Dysplastic" patterns in patients with cancer, but not such a high incidence as would be predicted on Wolfe's findings. The association between dysplastic patterns and ER positive tumours suggests hormonal promotion of both conditions.

Book review

La Xeromammografia. (*Xeromammography*). By G. Luzzatti, B. Salvadori and E. Tavani. pp. 237, 1979 (Excerpta Medica, Amsterdam Oxford; Piccin, Milan).
ISBN 90-129-0402

This book has been compiled from material obtained from 1973–1979 at the Department of Radiology of the Ospedal San Carlo Borremeo in Milan, correlating clinical, radiological and pathological aspects of the case material. Its major concern is to show the wide range of clinical material demonstrated by xeroradiography, but emphasizes the importance of accompanying clinical examination. The book is produced primarily for radiologists but is also intended to be of interest to clinicians.

The text is arranged in double columns, one in English alongside one in Italian. The print in the two columns is different in type, and the English is at times a little stilted. These factors necessitate additional concentration by the reader. The detailed descriptions are always separated from the illustrations by several pages, which also does not add to ease of correlation. There is a relatively short description of xeromammographic technique followed by a description of the normal xerographic appearances of the breasts at all ages. Next, the appearances of benign and malignant conditions and their related parenchymal changes are described. The book is concerned entirely with clinical problems and the authors have not discussed the use of xeroradiography in mass screening for breast cancer, nor the possible risks from ionizing radiation.

The illustrations are extremely good and emphasize the much better quality of xerograph reproduction than radiograph reproduction. The quality of the illustrations alone is such that this volume will be a valuable reference book for any department carrying out mammography be it with xeroradiography or by the standard film technique.

ZOË D. DAVIES.

1981, *British Journal of Radiology*, *54*, 168–171

Proceedings of The British Institute of Radiology

Symposium in honour of Dr. Frank Ellis, September 18, 1980

Held at the Radcliffe Infirmary, Oxford. Sponsored by the Radiobiology Committee of The British Institute of Radiology.

This meeting was organized at the initial suggestion of Professors H. D. Suit and E. J. Hall, in celebration of the 75th birthday of Dr. Frank Ellis and in consideration of his outstanding contributions to radiotherapy. An organizing committee included Professors R. J. Berry, L. G. Lajtha and A. H. W. Nias and Drs. J. M. Brindle and C. H. Paine. The Radiobiology Committee of the BIR kindly sponsored the scientific meeting which consisted of a series of invited papers, some presented by ex-pupils of Dr. Ellis and others upon topics which were known to be his particular interest. The morning was devoted principally to basic sciences and radiobiology, and the afternoon to the more clinical aspects of radiation therapy. The meeting proved to be a successful and pleasant occasion with over 100 participants from many countries, and was followed by a dinner at which speeches and presentations were made by a number of radiotherapists to their colleague who has contributed so much in this field.

Cell proliferation and loss as a basis for radiotherapy, by R. J. Berry.
Transformation of mammalian cells *in vitro*, by E. J. Hall.
Platinum drug-radiation interactions, by A. H. W. Nias.
Development of new hypoxic-cell radiosensitizers, by J. M. Brown.
Electron beam treatment planning, by J. S. Laughlin, A. Reid, R. Mohan and R. Riley.
Experiences with proton beam therapy in man, by H. D. Suit, M. Goitein, J. E. Munzenrider, Lynn Verhey, A. M. Koehler, W. U. Shipley and Rita M. Linggood.
Some aspects of brachytherapy in Oxford, by C. H. Paine.
Radiation and the maladie of Dupuytren, by J. M. Brindle.
NSD and its clinical relevance, by J. F. Fowler.
Three or five times weekly fractionation—evidence from the BIR fractionation survey of laryngeal carcinoma, by G. Wiernik.
Multiple daily fractions in radiotherapy, by V. H. J. Svoboda.

CELL PROLIFERATION AND LOSS AS A BASIS FOR RADIOTHERAPY

By R. J. Berry

Department of Medical Oncology,
Middlesex Hospital, London W1

Successful radiotherapy for the treatment of human tumours consists in administering to a localized tumour a given course of radiation which ablates the reproductive capacity of all the potentially proliferating tumour cells whilst remaining within the limits of normal tissue tolerance acceptable to the individual radiotherapist and his patient.

A number of biological factors modify both the tumour cell kill and the response of the dose-limiting normal tissues; these include the intrinsic radiosensitivity of the clonogenic tumour cells, their capacity for repair of sublethal radiation damage between dose fractions, the rate of tumour shrinkage during fractionated treatment and its effect on the nutrition and oxygenation of tumour cells, the capability (or not) of tumour "stem" cells to respond to their depletion by stimulated proliferation, etc. In addition the damage to limiting normal tissues will be determined by the volume of tissue irradiated, the proportion of normal tissue "stem" cells surviving the irradiation, their capacity for stimulated proliferation, the ability of adjacent unirradiated normal tissues to supply "stem" or differentiated cells by migration, etc.

It is argued that the most important single biological factor affecting success or failure in radiotherapy is the kinetics of cell proliferation and loss in the tumour and in the limiting normal tissues, and the changes which occur in these in response to and during fractionated treatment. Evidence is presented that the high rate of cell loss ascribed to the majority of human tumours of epithelial origin may be an artefact of technique. The consequences of widely differing rates of cell proliferation in human tumours and their changes in response to local and systemic therapy are discussed.

TRANSFORMATION OF MAMMALIAN CELLS *IN VITRO*

By E. J. Hall

College of Physicians and Surgeons,
Columbia University, New York, USA

In vitro assays for oncogenic transformation represent a powerful tool to identify and compare agents that are potentially carcinogenic. As a model system such assays also allow the basic mechanisms of carcinogenesis to be investigated.

Our experiments have involved the use of an established line of mouse fibroblasts (10T½), fresh explants of hamster embryo cells, and some preliminary work with cells of human origin. Three broad areas of research have been addressed using these systems.

First, the shape of the dose-response relationship for oncogenic transformation by X rays has been determined over a range of doses from 0·01 to 10 Gy. The complex shape of the dose-response relationship implies that the estimation of the transformation incidence at low doses by a linear extrapolation from high dose data is not necessarily valid. Furthermore, over a certain low-dose range, splitting of the dose into several fractions, or delivery of the dose at low dose-rate, leads to an *enhancement* of the transformation incidence compared with that obtained for the same total dose delivered in a single acute exposure. These results have far reaching implications in radiation protection and in the development of risk estimates for radiation-induced carcinogenesis.

Second, *in vitro* oncogenic transformation has also proved to be useful to compare the potential carcinogenicity of the new generation of hypoxic-cell radiosensitizers. It has been found, for example, that compounds with similar sensitizing efficiency may differ widely in the transformation incidence they produce, depending upon their chemical structure.

Third, a wide variety of commonly used chemotherapy agents have been screened using the transformation assays. It is no surprise to find that the agents tested vary widely in the extent to which they produce transformation, but many are much more potent carcinogens than radiation.

PLATINUM DRUG-RADIATION INTERACTIONS

By A. H. W. Nias

Richard Dimbleby Department of Cancer Research,
St. Thomas' Hospital, London SE1

When drug therapy is combined with radiotherapy there are a number of possible interactions ranging from radiation protection at one extreme to radiosensitization at the other, depending upon the drug and the time/dose regime. In order to determine the true extent of such interactions it is first necessary to obtain complete dose-response curves for drug alone and radiation alone. The effect of therapy can then be assayed for each of the possible combinations of dose and time intervals. A significant degree of enhancement may then be found for certain combinations but not for others.

Platinum co-ordination complexes are cytotoxic drugs with a mode of action analogous to alklyating agents. The original drug Cis-PDD is used in the chemotherapy of ovarian and testicular tumours, often as a single agent, but nephrotoxicity is dose limiting. A number of second generation platinum complexes have been synthesized. Cis-PAD has a very high therapeutic ratio in laboratory tumour tests but is very insoluble. CHIP has a lower therapeutic ratio but is very soluble and shows minimal nephrotoxicity in animal tests.

Combinations of X-irradiation and either Cis-PAD or CHIP have been tested *in vitro* using CHO cell cultures. Dose-modifying factors have been determined for the radiation dose-response curves of aerated cells pre-treated with different doses of Cis-PAD at different time intervals. Isobolographic analysis of the data has also been used to indicate the most synergistic regime. Dose modification is also found when hypoxic cells are pre-treated with CHIP and this compares favourably with the DMF for aerated cells treated with the same time/dose regime. Other regimes show less therapeutic advantage.

This research is supported by the Cancer Research Campaign.

DEVELOPMENT OF NEW HYPOXIC-CELL RADIOSENSITIZERS

By J. M. Brown

Department of Radiology, Stanford University
Medical Center, California, USA

Misonidazole, the current hypoxic-cell radiosensitizer in clinical trials, produces neurotoxicity in patients, and this limits the dose that can be given to roughly 1/5 to 1/10 of that needed for maximum radiosensitization of the hypoxic cells. We have explored different structural analogues of the 2-nitroimidazole, misonidazole, in an attempt to overcome this problem. The rationale has been to use the fact that radiosensitization of the hypoxic tumour cells depends on peak concentration of the sensitizer in these cells, whereas toxicity to the neural tissues depends on total exposure of these tissues to the drug. By reducing the lipid solubility of 2-nitroimidazoles below that of misonidazole we have been able to inhibit drug penetration across the blood-brain and blood-nerve barriers without affecting penetration into the tumour. This has led to radiosensitizers which are equally as efficient as misonidazole in radiosensitizing tumour cells *in vivo* but which are less neurotoxic as judged by functional endpoints.

In order to select the optimum compound in this series, we have used a combination of radiosensitization experiments *in vivo* and *in vitro*, and pharmacokinetic studies. We have found that lipid solubility cannot be reduced below an octanol water partition co-efficient of 0·04 without losing radiosensitization both *in vivo* and *in vitro*. Studies of the rate of diffusion of these compounds across the cell membrane have shown that this loss of radiosensitization is due to slow and inadequate build up of sensitizer within the cell. However, there is little or no barrier to the rapid distribution of these radiosensitizers throughout tumours, including penetration to the radioresistant hypoxic cells.

Based on these studies we have identified two new 2-nitroimidazoles, SR–2508 and SR–2555, as prime candidates for replacements for misonidazole in the clinic. Whichever is finally selected (based on large-animal toxicity studies currently in progress) should be able to be given at high enough doses to achieve full radiosensitization of the hypoxic tumour cells.

ELECTRON BEAM TREATMENT PLANNING

By J. S. Laughlin, A. Reid, R. Mohan, and R. Riley

Biophysics Laboratory, Memorial Sloan-Kettering
Cancer Center, New York, USA

At present we are using a semi-empirical model developed here for routine treatment-planning purposes. The model is based on the measured characteristics of the radiation dose distributions in phantoms using tissue maximum and off-centre ratios for different SSD's to establish the appropriate distance-dependence factors. This model is used in conjunction with CT data where CT numbers are converted into effective electron density ratios and then pixel by pixel corrections are made automatically for all internal inhomogeneities.

Illustrations demonstrating this will be shown for patients undergoing total-body irradiation prior to bone-marrow transplantation where both photons and electrons are employed and dose versus area/volume assessments in lung are made.

Work is at present in progress on alternative methods to provide better modelling for the effects of small inhomogeneities using pencil-beam integration with the pencil beams being generated by various techniques including Monte Carlo calculations.

EXPERIENCES WITH PROTON BEAM THERAPY IN MAN

By H. D. Suit, M. Goitein, J. E. Munzenrider,
Lynn Verhey, A. M. Koehler, W. U. Shipley,
and Rita M. Linggood

Department of Radiation Medicine,
Massachusetts General Hospital, Boston, USA

Experience at the Massachusetts General Hospital and Harvard Cyclotron Laboratory using a modulated-energy proton beam in the definitive treatment of 203 cancer patients shows that this is a technically feasible and attractive modality. Importantly, for the patients treated we have employed smaller treatment volumes and administered higher total doses than would have been obtained by employing photon techniques as used in our institution. Our judgement is that reactions of normal tissues have with quite few exceptions been readily tolerated despite the higher dose to the target volume. The results in terms of local control have been highly encouraging and are not surprising in view of the increment in total dose administered. The entire advantage for proton-beam radiation therapy lies in the use of a smaller treatment volume which means an increased tolerance and therefore higher doses to the target are feasible. We are now entering the phase of initiation of prospective randomized clinical trials. The first two trials are for carcinoma of the prostate, carcinoma of the oral cavity and oral pharynx.

SOME ASPECTS OF BRACHYTHERAPY IN OXFORD

By C. H. Paine

Department of Radiotherapy and Oncology,
Churchill Hospital, Oxford

The curability of suitable small tumours by interstitial radiotherapy has not been lost sight of in the Oxford department since its founder, Frank Ellis, retired. Although only about half the number of implants (or moulds) were carried out in 1979 as in 1969, mainly because of the introduction of electron therapy, the indications for such treatment have broadened to include more breast cases, and the training of junior staff is considered most important.

Radium and radon are no longer in use in this unit, having been replaced by iridium-192 wire using the after-loading techniques largely originated by the late Ulrich Henschke and by Bernard Pierquin (Paine, 1972), but modified for some special applications (which will be mentioned) in Oxford.

It is the author's view that one of the attractions of the Oxford implantation method is the simplicity of its dosimetry—based on the teaching of Frank Ellis that implants should be so planned and constructed that the resultant isodoses enclose the target volume, and using the crossline data (with minor modernizations) of Hall, *et al.* (1966). Some of the principles of the Paris method of dosimetry are also incorporated (Pierquin *et al.*, 1978). This communication will include a brief description of current Oxford implant dosimetry.

REFERENCES

Paine, C. H., 1972. Modern after-loading methods in interstitial radiotherapy. *Clinical Radiology, 23,* 263–272.

Hall, E. J., Oliver, R., and Shepstone, B. J., 1966. Routine dosimetry with tantalum-182 and iridium-192 wires. *Acta Radiologica 4,* 155–160.

Pierquin, B., Dutreix, A., Paine, C. H., Chassagne, D., Marinello, G. and Ash, D., 1978. The Paris System in interstitial radiotherapy. *Acta Radiologica Oncology, 17,* 33–47.

RADIATION AND THE MALADIE OF DUPUYTREN

By J. M. Brindle

Department of Radiotherapy and Oncology,
Plymouth General Hospital

A common disease, the aetiology of which remains almost as obscure as 150 years ago (Dupuytren, 1832), provides an example of the possible usefulness of low-dosage irradiation in a non-malignant condition. Surgery, except in expert hands, may produce more problems than solutions (Hueston, 1963).

Frank Ellis developed a technique of radiotherapy which has been used by the author since 1965. Thirty-six patients have been assessed at five years and a further twenty patients have been treated since 1975 and are still under review.

The value of this technique is discussed and comments made on the risks of late tumour induction (MRC Radiobiology Forum, 1972). Should ionising radiation be used for treatment of diseases other than cancer?

REFERENCES

Dupuytren, G., 1832. Quoted by Pulvertaft, R. G. and Campbell Reid, D. A., 1963. *British Journal of Surgery, 1,* 683.

Hueston, J. T., 1963. Dupuytren's Contracture. (E. & S. Livingstone, Edinburgh and London).

MRC Radiobiology Forum on Radiological Protection and the Skin, 1972. *British Journal of Radiology, 45,* 610–620.

NSD AND ITS CLINICAL RELEVANCE

By J. F. Fowler

Gray Laboratory, Mount Vernon Hospital,
Northwood, Middlesex

The Nominal Standard Dose formula proposed by Dr. Frank Ellis in 1969 formalized the separate factors of fraction number and overall time for tolerance doses to normal tissue as follows:

$$\text{Total Dose} = \text{NSD} \times N^{0.24} \times T^{0.11}$$

It was derived from clinical data and agreed with results from acute and medium-term reactions in the skin of pigs.

The NSD formula has been much used clinically, and it has undoubtedly saved many patients from being given wrong doses, within the limits of use described below. At the same time the "straight log-log line" formulation has been a challenge to radiobiologists to try to disprove it and to clinicians to obtain human data which might enable the formula to be modified.

Although neither the fraction number nor the time exponent can (of course) be exactly constant, the extent of their discrepancies is not great and therefore divergences from the NSD formula have taken a long time to emerge. The approximations were good ones, and several systems have been derived from them, notably TDF and CRE. The NSD formula still holds good for acute reactions in skin over the originally suggested range of 4–30 fractions and up to about 100 days overall time. However, for late reactions in skin and in other normal tissues smaller total doses are tolerated for a few big fractions than are predicted by the NSD formula.

If limited now to 10–30 fractions, and to overall times not exceeding six weeks, the NSD formula is still a useful first check on whether a proposed dose change is reasonable. It now appears that the fraction number exponent is greater than 0·24 for a few big fractions and smaller for many small fractions. The time exponent is smaller than 0·11 for late-occurring damage, *i.e.* in tissues which do not proliferate significantly during the weeks of treatment. The NSD formula does not contain a volume factor because the intention was not to provide a "general dose recommendation" in radiotherapy, but only to enable an experienced clinician to modify his dose level if he wished to change only the number of fractions or the overall time.

THREE OR FIVE TIMES WEEKLY FRACTIONATION—EVIDENCE FROM THE BIR FRACTIONATION SURVEY OF LARYNGEAL CARCINOMA

By G. Wiernik

Department of Radiotherapy and Oncology
Churchill Hospital, Oxford

Treatment three instead of five times per week offers considerable benefit to the patient as well as being financially attractive. The correct interpretation of the BIR trial is, therefore, of great importance.

A total of 732 patients was entered into the BIR fractionation study (Wiernik *et al.*, 1978) and of these 281 patients had glottic disease with a high cure rate, *i.e.* T1 tumours according to the TNM classification. Though survival rates are similar in both arms of the trial, it is possible to identify differences in the biological effects of the two fractionation regimes in only this restricted group where the recurrence-free rate appears to be significantly better in the patients given daily treatment. No such difference has been demonstrated in the patients with more advanced laryngeal or with pharyngeal tumours. A number of factors have to be considered for the correct evaluation of this study.

Because the trial was based on the "null-hypothesis", the difference in results may be due to improved tumour control from a marginal mis-matching of the biological effect of the two regimes. Recently published experimental data, based on a large-animal model (Hopewell *et al.*, 1979), have shown that iso-effect plots of fractionation exponents are not linear but have slopes which may vary by 300% for different numbers of fractions, and this could account for the differences that have been observed. On the other hand wide variations have been reported for the steepness of the slope of dose-response curves for tumours, and this is, of course, reflected in the therapeutic ratio. This problem is compounded by the lack of suitable, quantitative methods for evaluating radiation damage in normal tissues which themselves appear to play a major role in tumour response (Wiernik, 1980). The relative importance of these various factors will be discussed.

REFERENCES

HOPEWELL, J. W., FOSTER, J. L., YOUNG, C. M. A., and WEIRNIK, G., 1979. Late radiation damage to pig skin. *Radiology*, *130*, 783–788.

WEIRNIK, G., 1980. Lessons from a multicentre clinical trial monitoring tumour and normal tissue response quantitatively. *British Journal of Cancer*, *41*, Suppl. IV, 51.

WIERNIK, G., BLEEHEN, N. M., BRINDLE, J., BULLIMORE, J., CHURCHILL-DAVIDSON, I. F. J., DAVIDSON, J., FOWLER, J. F., FRANCIS, P., HADDEN, R. C. M., HAYBITTLE, J. L., HOWARD, N., LANSLEY, I. F., LINDUP, R., PHILLIPS, D. L. and SKEGGS, D., 1978. Sixth Interim Progress Report of The British Institute of Radiology fractionation study of 3F/week versus 5F/week in radiotherapy of the laryngopharynx. *British Journal of Radiology*, *51*, 241–250.

MULTIPLE DAILY FRACTIONS IN RADIOTHERAPY

By V. H. J. Svoboda

Department of Radiotherapy and Oncology,
St. Mary's Hospital, Portsmouth

Fractions of conventional size (160–230 cGy (rad)) are employed in 5–14 days overall time, and three or four treatments per day. The minimal interval between the sessions is three hours. After 2600 cGy superficial therapy split into two fractions, the acute skin reaction will be the same, whether the interval is 24 or three hours. Also, when giving megavoltage treatments to large volumes, the day-long interval between fractions can be reduced to three hours, treating three sessions in a day. Eight years' experience with such treatment in breast cancer has made it possible to construct a table of tolerances (Table I), plotting the number of sessions against overall time in days. Some tumours of the head and neck were treated similarly. After a minimum of three years' follow-up, six patients who received 5 500 cGy in 27 sessions over 11 days to the larynx showed no signs of late damage. The risk in this method is uncertainty about the fraction size and the time factor. Over-fractionation and split courses designed to try to avoid acute reaction increase the risk of late damage, and the use of small fractions can result in inadequate tumour control. Multiple daily fractions for squamous carcinoma should be designed near the tolerance level.

Almost all advanced breast tumours responded. Two-thirds showed complete local control and half of these responses were long lasting. Thus, in 5–12 day treatment periods, similar results were obtained as would be expected with 21–70 day regimes. Out of 53 patients with mostly advanced squamous carcinoma of the head and neck, 43 responded completely to a 12 day course, seven could not yet be assessed, and in three the response was only partial. Two of them did not receive the full dose. Misonidazole, which was used in eight patients, did not modify the response. Similar favourable responses were obtained with squamous carcinoma localized elsewhere. Multiple daily fractionation offers a better therapeutic ratio for squamous carcinoma than conventional radiotherapy. It is well tolerated and practicable within the seven hour working day. It brings rapid relief of symptoms, needs only brief hospitalization, and the reactions heal fast.

TABLE I

WHOLE BREAST AND GLANDULAR AREAS TANGENT PAIR OF LARGE COBALT FIELDS. SKIN, BREAST AND MUSCLE CHANGES AT 18 MONTHS OR LATER.

Reaction score*	Fractionation (fractions/days)							
3			15/5	15/9				25/35
			20/5					
2			20/8	20/5	24/10			25/70
			15/21	24/10				
		15/5	24/10	30/12		30/42		
1		20/5	30/12	32/12		25/70		
							50/35	
0	15/5		32/10				50/70	50/70
Tumour dose (cGy)	4000	4250	4500	4750	5000	5500	6000	6500

*Reaction score scale
3—Skin leathering and muscle fibrosis, or necrosis of bone, skin or pleural scarring.
2—Moderate skin thickening and muscle fibrosis.
1—Mild skin thickening.
0—Normal appearances.

Vol. 54, No. 638

Proceedings of The British Institute of Radiology

Silverless X-ray imaging

Abstracts of papers presented at a meeting held on Thursday, October 16th 1980 at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

Chairman: Mr. G. R. Higson

Radiological requirements from non-silver imaging systems, by J. D. Spencer.
An introduction to the principles of ionography, by J. W. Boag.
Digital radiology, by B. R. Pullan.
Imaging characteristics in ionography, by A. Rheude.

RADIOLOGICAL REQUIREMENTS FROM NON-SILVER IMAGING SYSTEMS

By J. D. Spencer

Northwick Park Hospital, Harrow, Middlesex

Despite the development over the last ten years of ultrasound, computed tomography, radionuclide imaging and improved image intensification systems, the demand for and cost of X-ray film has increased year by year. It is evident therefore that although these newer techniques have replaced some traditional X-ray examinations there is a continuing and increasing requirement for area X-ray imaging.

A traditional approach to radiological imaging requirements involves consideration of the area covered by a system, the resolution and artefacts produced, and the radiation dose involved. In addition, the "edge effect" is important when considering Xeroradiography and Ionography.

A graph of the number of films used against the size of the films for Northwick Park Hospital 1979–1980 reveals two peaks, one at 700–800 sq. cm. (barium meals, oral cholecystograms, extremities) and one at 1200–1600 sq. cm (IVP, barium enemas, chests, abdomens). The most "popular" film sizes in terms of the total area covered are the 35 by 43 and 40 by 40 cm films. The effect of any alternative system on the total use of film has to be seen against this background.

The question of "resolution" is more complex as it involves unsharpness, contrast, modulation transfer function, noise, line pair resolution and latitude. Examples of radiographs of specimens of lung, breast and colon demonstrate that, even with the best film, radiologists can only see a small proportion of the pathology present. Any further deterioration in conventional film image quality resulting from the use of less silver would be undesirable. A requirement for 10 line pairs per mm can be identified and occasionally, as in abdominal angiography, this resolution is required over a large area.

The problem of radiation dose should be considered in relation to the benefit to the patient and this is best left to the radiologist to decide in the context of the seriousness and complexity of the diagnostic problem. An alternative system which allowed the radiologist to increase the resolution and dose when justified would be preferable to a system with fixed resolution and dose.

A more radical approach to radiological requirements can be considered. A "real time" area imaging system such as fluoroscopy would meet most radiological requirements if the resolution was improved. In addition such a system would allow instant reporting and perhaps remove the necessity for a hard copy of the image. Small area high resolution industrial X-ray TV cameras exist (*e.g.* Hamamatsu N603) and an increase in size to 10 by 10 cm would fulfil at least 36 medical imaging applications, mainly in ENT, Dental, Paediatric and A & E radiology. The possibility of digitising large area images is considered unlikely to be helpful in terms of image manipulation and interpretation since the attenuation values assigned to each picture element would be derived from the average of many different organs and structures within the body.

AN INTRODUCTION TO THE PRINCIPLES OF IONOGRAPHY

By J. W. Boag

40 Overton Road, Sutton, Surrey SM2 6QR

Very early attempts at ionography (Thompson, 1896; Righi, 1903) were not pursued further, but interest was renewed by the publication of a paper (Reiss, 1965) describing the use of a thin gas layer and of electron avalanche amplification to increase sensitivity. This method was not entirely successful and modern ionographic equipment employs the principle of absorbing the X-ray photons in a thick layer of a high-Z gas, usually at a pressure of several atmospheres (Johns *et al.*, 1974). The ejected photoelectrons ionize the gas and these ions are collected by a strong electric field between the electrodes and accumulate on an insulating foil stretched over one electrode. The charge pattern on the foil represents the "latent image" in ionography and this can be developed —*i.e.* made visible—in various ways. The simple idea which makes possible good resolution, despite a thick absorbing layer, is to design the latter as a spherical shell centred on the X-ray target. This requires a rigid coupling between the X-ray tube and the ionographic chamber so the system has to be dedicated to a particular type of investigation, *e.g.* mammography, or chest radiography. Although the most energetic photoelectrons may have a range of more than 1 mm in xenon at ten atmospheres it is usually possible to resolve about 10 l.p./mm provided that ions and not free electrons are collected to form the image. The reasons for this have been described (Johns *et al.*, 1974). Various development methods can be used. Exposure to a powder aerosol, as in xeroradiography, gives strong edge contrast pictures, while immersion in a liquid "toner" yields a density image which is viewed by transmitted light, and which is very similar to a normal X-ray film.

REFERENCES

Johns, H. E., Fenster, A., Plewes, D., Boag, J. W. and Jeffery, P. N., 1974. Gas ionization methods of electrostatic image formation in radiography. *British Journal of Radiology*, *47*, 519.

Reiss, K. H., 1965. Pictorial representation of ionizing radiation by electrostatic storage of electron avalanches. *Zeitschrift. für angewandte Physik*, *19*, 1.

Righi, A., 1903. The movement of ions in the electric field. 1st Edn. (Zanichelli, Bologna).

Thompson, S. P., 1896. Electric shadows and luminescence. *Royal Institution (London) Discourses*, *15*, 191.

Proceedings of The British Institute of Radiology

IMAGING CHARACTERISTICS IN IONOGRAPHY

By Alfred Rheude

Agfa-Gevaert AG, Camera-Werk, Munich

Ionography is an electrostatic imaging process which produces a charge pattern on a dielectric surface as a function of the intensity and the spatial distribution of the X-ray exposure. Visualization of the latent image is carried out by methods well-known in electrophotography, *e.g.* by electrophoretic toner deposition upon the receptor. This paper stresses the practical aspects of optimizing the design parameters when ionography is used in mammography and in chest-radiography.

The speed of latent image formation is determined by the properties of the absorber and by the efficiency with which the charges produced can be collected. The surface charge on the receptor is converted into an optical density by the development process. Its speed depends upon the toner properties, the receptor capacitance and the process parameters. The overall speed of the system is the product of the sensitivities for charge collection and for development. The rate of image charge neutralization determines whether the final image shall appear as continuous tone reproduction or with edge enhancement. The ionographic imaging process can be summarized in a classical four-quadrant representation. The image quality and speed achieved are equivalent to screen/film systems for both the above types of X-ray examinations. Several problems in operation and in the properties of the materials used have to be solved before ionography can become competitive with silver-halide film in medical radiography.

DIGITAL RADIOGRAPHY

By B. R. Pullan

Department of Medical Biophysics
University of Manchester, Manchester, UK

In digital radiography the distribution of X-ray flux emerging from a patient is measured with high quantum-efficiency detectors. The measured distribution is digitized and stored in a computer for subsequent processing and display. The dynamic range of the recorded measurements is large at acceptable radiation doses and processing is necessary to allow visualization of clinically meaningful small changes. A number of processing techniques can be applied such as edge enhancement and subtraction. Digital subtraction radiography using intravenous contrast agents is a promising approach. Theoretical calculations show that with an optimal unit quantum-efficiency system cerebral vessels should be visible down to 1 mm in diameter with a concentration of only 1.5 mg/ml of iodine at a radiation dose of 1 rad. Experiments have shown that such concentrations can probably be achieved by intravenous bolus injection. It has also been shown that subtraction imaging using intravenous contrast media will require two-dimensional detection systems. Two approaches appear feasible: one using digitized signals from an image intensifier—and the other using electrically read ionographic plates. Both approaches are being studied.

Book reviews

Das Röntgenbild (*The Radiograph: Theory, Methodology, Techniques, Guidelines for training and applications*). By R. Felix and B. Ramm. pp. 255, 95 figs, 11 tables, 1980. (Georg Thieme, Stuttgart/New York), DM 19.80.
ISBN 3-13-5740-01-3

This small pocket book contains a remarkable range of valuable information on all aspects of diagnostic radiology. The attempt to cover the whole field from basic physics to clinical techniques, including CT and ultrasound, within the compass of 250 pages might well lead a reader to expect a very superficial treatment. However, the authors, who are both professors of clinical radiology, have achieved a concise but accurate treatment of the basic physics as well as of the apparatus and techniques. Where simplified explanations are necessary these are presented without "talking down" to the reader and the necessary mathematical formulae are not avoided. The authors acknowledge the assistance of no fewer than 29 colleagues in the preparation of the book and this has doubtless helped to eliminate errors. Despite its conciseness the text has style and is easily readable. The detailed list of contents and the extensive index make it easy to find a particular section or formula. An unusual feature is a detachable page at the end of the volume with a list of questions to elicit readers' comments, criticisms or corrections. Other authors and publishers might copy! The price is reasonable and the book is likely to prove an indispensable *vade mecum* for the young radiologist who can read German.

J. W. Boag.

Illustrated Guide to X-ray Technics By John E. Cullinan and Angeline M. Cullinan. 2nd Ed. pp.xiii+234, 1980 (J. B. Lippincott Co; Harper and Row, London), £17·95.
ISBN 0-397-50425-X

This is an excellent book dealing with many aspects of radiographic equipment, photography and technique. It is written in an interesting and concise manner with many diagrams and radiographs to help the reader understand the text.

The aim of the book is to help those involved in radiology and radiography to understand the equipment and accessories at their disposal and use them to produce good quality diagnostic films. It contains much practical information not mentioned in other books.

The second edition has been brought up to date. The chapters have been re-arranged, some altered and some rewritten, and there are two new chapters on the art of positioning and radiography of the chest.

This book would be helpful to trainee radiologists, teachers of radiography and radiographers taking their Higher Diploma. It also deserves a place in the X-ray Department and School of Radiography library.

E. A. Pollard.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

International Fellowships

The International Union Against Cancer, with funds provided by the Cancer Research Campaign (UK), will award fellowships for research on cancer, designed to enable investigators to work abroad for a period. The duration of the fellowships ordinarily will be one year. Applications and supporting documents to be received by mid-February 1981. Application forms and information from: International Union Against Cancer, rue du Conseil-Général, 3, 1205 Geneva, Switzerland.

Radioisotopes in Gastroenterology

An all-day meeting, organized by the BIR Nuclear Medicine Committee and starting at 9.30 a.m., will be held on Wednesday, February 18 at the Institute House, 32 Welbeck Street, London W1. Proffered papers on gastric emptying, bile acid metabolism, hepatobiliary scintigraphy, absorption studies. Enquiries to Dr. M. V. Merrick, Western General Hospital, Edinburgh EH4 2XU.

Silvanus Thompson Memorial Lecture

Will be held at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG on February 18, 1981 at 6.00 p.m. Professor J. R. Mallard will speak on "The Noes have it—do they?"

Radionuclides in Gastroenterology

An all-day meeting to be held on February 18, 1981 organized by the Nuclear Medicine Committee of The British Institute of Radiology, at Institute House, 32 Welbeck Street, London W1M 7PG (01–935 6237). Further information from the General Secretary.

State of the Art Seminar: Management of Metastatic Malignancy—Can Adult Oncology Learn from the Paediatric Field?

A meeting to be chaired by Dr. Dorothy Pearson will be held at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, on February 19, 1981 at 5.45 p.m. For further information contact the General Secretary.

Combined Radiotherapy and Chemotherapy: Advantages, Disadvantages—Can Radiobiology Help?

An evening meeting to be held on February 19, 1981, organized jointly with the Royal Society of Medicine (Section of Radiology) and the Royal College of Radiologists. Speakers: Drs. D. P. Deakin, J. Moore, Dorothy Pearson and Ruth Sandland. 32 Welbeck Street, London W1.

BIR Radiobiology Meeting

There will be a general radiobiology Work-in-Progress meeting at 11.00 a.m. in the Institute on February 20, 1981.

Symposium on Colorectal Cancer

To be held on February 27–28, 1981 at Jarvis Hall, 66 Portland Place, London W1. A multi-disciplinary symposium organized by the Royal College of Radiologists and intended for consultants, senior registrars and research workers, but open to all interested medical practitioners. Registration fee £25·00. Full details from The Meetings Secretary, RCR, 38 Portland Place, London W1N 3DG.

West of Scotland Committee for Postgraduate Medical Education Intensive Course in Clinical Oncology and Radiotherapeutics

March 9–13, 1981. An intensive five-day course suitable for candidates preparing for the F.R.C.R. Part II examination will be held in the Glasgow Institute of Radiotherapeutics (Western Infirmary and Belvidere Hospital). The programme will include tutorial sessions, case presentations and discussions on topics related to recent advances. Application forms from: Mrs. E. A. McPherson, Administrative Assistant, University of Glasgow, Glasgow G12 8QQ.

Radiographic Systems: What is Best?

An all day meeting is to be held at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG on March 18, 1981. Speakers: Prof. B. R. Pullan, Drs. G. M. Ardran, J. H. E. Carmichael, D. H. Trapnell and G. R. Higson. For further information contact the General Secretary.

International Symposium of Body CT

Colegio Oficial de Médicos, po. Bonanova, 47, Barcelona, Spain. April 2, 3 and 4, 1981. Speakers: Professors R. J. Alfidi, A. Baert, J. M. Domenich, L. Kreel, J. L. Lamarque, P. Rossi; Drs. Th. Falke, G. Hansen, J. Husband, M. Robles, Pedrosa, J. Peri, J. M. Rius, M. Rovira, F. Sanchiz, C. Sanpons, Sureda and Van Voorthuisen.

Registration: before March 1, $150; after March 1, $220; residents (who must have a letter from the Chief of their training programme), $80 and $120; cost to include meetings, lunch, dinner and diploma. Write to: Centro Radiologico Computerizado de Barcelona, c/Tavern, 82, Barcelona-6, Spain.

Spring Meeting, BIR/RCR/RSM

A joint Spring Meeting, organized by the Royal College of Radiologists, will be held in Bristol on April 3–4, 1981. For further information contact the General Secretary, the Royal College of Radiologists, 38 Portland Place, London W1.

BIR Annual Congress 1981 and Scientific Exhibition

The British Institute of Radiology Annual Congress will be held on April 9–10, 1981 at the Royal Free Hospital and will include the Mackenzie Davidson Memorial Lecture by R. G. Grainger on "Intravascular contrast media—present perspectives". Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

Physics in Medical Ultrasound

Durham, April 13–14, 1981

This meeting, organized by the HPA Ultrasonics Topic Group in association with the British Medical Ultrasound Society, is intended to provide a forum for the presentation and discussion of scientific and technical aspects of ultrasound in medicine, and will be accompanied by an exhibition of commercial test and research equipment. Accommodation available. Information: Dr. T. A. Whittingham, Regional Medical Physics Department, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE.

Forthcoming events and notices

Echocardiography

A course in Echocardiography will be held at Harefield Hospital from April 27 to May 1, 1981. The course is intended for those having experience in cardiac ultrasound and working in the field. Accommodation available. Further details from Mrs. M. Beech, telephone Harefield 3737, ext. 609.

Fourth European Congress on Ultrasonics in Medicine

This will be held in Dubrovnik, May 17–24, 1981, sponsored by EFSUMB and organized by the Yugoslav Association of Societies for Ultrasound in Medicine and Biology. Information from Dr. Višnja Latin, M.D., D.Sc., President of the Organizing Committee, Jagode Truhelke, 26, 41090 Zagreb, Yugoslavia.

Clinical Radiotherapy and Oncology

A course in Clinical Radiotherapy and Oncology will be held at this hospital from Monday June 8 to Friday June 12 1981. The course is designed for radiotherapists in training and those wishing an introduction to Christie Hospital techniques. Sessions by the Consultant Staff will include discussion of the management of head and neck, cervix (including afterloading), breast, skin, CNS and testicular tumours.

Application forms for places, which will be limited, should be sent to Dr. R. D. Hunter, Consultant Radiotherapist, Christie Hospital and Holt Radium Institute, from whom details may be obtained. Registration fee £20.

Fifth Congress of the European Nuclear Medicine Society

Nineteenth Congress of the Societa Italiana di Biologia e Medicina Nucleare

Pisa, June 9–12, 1981. Main suggested topics: cardiovascular applications of radionuclides *in vivo* and *in vitro*; advances in regional lung morphofunctional studies; development of radioimmunoassay in comparison with non-radioactive immunochemical techniques; advances in nuclear imaging in comparison with alternative techniques. Official language: English. There will also be an industrial and technical exhibition.

Registration forms and other information from: The Organizing Secretariat, OIC, Via G. Modena 19, 50121 Florence, Italy. (Registration by April 15, 1981).

Radiology of the Small Intestine

A one-day course will be held on Wednesday, June 17, 1981 at the John Radcliffe Hospital, Oxford. Registration fee £21·00. For further details contact: Dr. D. J. Nolan, Department of Radiology, John Radcliffe Hospital, Oxford OX3 9DU (phone (0865) 817238).

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Programme from: ICR81, c/o Brussels International Trade Fair, Parc des Expositions B-1020, Brussels, Belgium.

First International Symposium on Minimal Invasive Cancer

Organized by the University Clinic of Obstetrics and Gynaecology, Graz, Austria, to be held at the Kongresshaus, Graz, July 1–4, 1981. Language: English. Main topics: cervix, vulva, endometrium, breast, oesophagus, stomach, large intestine, lung, thyroid, urinary bladder, prostate, larynx, oral cavity, skin, other organs. Enquiries: Interconvention, PO Box 105, A-1014, Vienna, Austria (phone (0222) 57 62 88). President: Prof. E. Burghardt; Secretary General, Dr. E. Holzer.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

Prospective Methods of Radiation Therapy in Developing Countries

The International Atomic Energy Agency will hold a seminar in Kyoto, Japan, August 31–September 4, 1981, intended for senior radiobiologists and/or medical doctors. The main objects are to review and discuss possible physical chemical and biological methods to improve the results of radiation therapy comparable to high LET radiation, and to stimulate research. Working language: English.

Information from D. A. Herbert, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4QJ. Applications and abstracts by March 15.

Radionuclides in Nephrology

Fifth International Symposium

September 2–4, 1981, at The Royal Society, London. Further details from A. R. Constable, Institute of Urology, 172 Shaftesbury Avenue, London WC2 8JE. Closing date for abstracts April 20.

Skeletal Radiology

The Eighth Refresher Course of the International Skeletal Society will be given in Madrid, Spain, September 25–27, 1981.

For further information, please write to: A. Bonakdarpour, M.D. Department of Diagnostic Radiology, Temple University Hospital, 3401 North Broad Street, Philadelphia, PA 19140, USA; or Prof. Dr. Friedrich W. Heuck, Zentrales Röntgeninstitut, Katharinen Hospital der Stadt Stuttgart, Kriegsbergstrasse 60, Stuttgart 1, Germany.

European Association of Radiology

II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

Radiology of the Mediastinum

4th Postgraduate Course in Radiology "P. Perona"

Will be held in Verona, Italy, October 1–3, 1981, organized by the Institute of Radiology of the University of Verona, the Italian Society of Radiology, and the College d'Enseignement Post-Universitaire en Radiologie. Simultaneous English/French translation. Registration L.65000. Information: Radiology Department, University Hospital, Verona (phone 045/582445).

Symposium of Radiological Physicists

Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

Symposium on Education and Training in Radiobiology

Dresden, May 12–15, 1982. Organized by the Gesellschaft für medizinische Radiologie der DDR, under the auspices of the European Society of Radiology. Languages: English, French and German. Registration by December 1, 1981;

papers by August 15, 1981. Information: Professor R. Barke, Radiologische Klinik, DDR – 8019, Dresden, Fetscherstrasse 74.

3RD WORLD FEDERATION MEETING FOR ULTRASOUND IN MEDICINE AND BIOLOGY: JULY 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01-486 6582).

3RD WORLD CONGRESS OF NUCLEAR MEDICINE AND BIOLOGY

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

BRUSSELS SYMPOSIUM ON ULTRASONOGRAPHY AND CANCER, SEPTEMBER 1982—CALL FOR PAPERS

Papers are invited on applications (experimental, diagnostic and therapeutic) of ultrasound in cancer. Abstracts (200–300 words) of proffered papers, containing all the important information, to be submitted before May 15, 1981. Full papers (if accepted) to arrive before November 10; they will be published in book form and available at the symposium. Conference organizer: Dr. S. Levi, Obstetrics and Gynaecology Department, Ultrasonography Department, University Hospital Brugmann, B-1020 Brussels, Belgium.

Obituary

Hubert E. Jones, B.Sc., M.B., B.Ch., D.M.R.D.

Dr. Hubert E. Jones, who was the Senior Radiologist at the Caernarvon and Anglesey General Hospital, Bangor, died on September 15 at the age of 56.

Hubert Edward Jones was born on March 10, 1924 in Pontypridd, Glamorganshire, was educated at Pontypridd Grammar School, University College, Cardiff, where he gained his B.Sc. in chemistry in 1944 and graduated M.B., B.Ch. from the Welsh National School of Medicine in 1947. After resident posts at Llandough, Sully and the Royal Gwent Hospitals, he joined the Royal Navy on a Short Service Commission serving as a Surgeon Lieutenant in the Far East during the Korean War. On completion of five years in the Navy he entered the Liverpool Royal Infirmary where after gaining his D.M.R.D. he became a Senior Registrar in Diagnostic Radiology and worked also at the Liverpool E.N.T. Infirmary and the Royal Children's Hospital, Liverpool. In January 1958 he was appointed Consultant Radiologist at Bangor.

For 16 years he worked single-handed in administrative charge of one large and seven smaller diagnostic radiology departments. During these and subsequent years, due largely to his unstinting efforts, the facilities increased to include a total of 11 smaller units as well as the main unit offering facilities including angiography, lymphangiography, ultrasound and radio-isotope scanning techniques. In 1960 he published an article on the radiology of the adrenal glands.

In addition to his work as a radiologist, he worked unceasingly to improve all aspects of medicine in Gwynedd through his extensive committee work. He had been Chairman of the Medical Executive and Area Medical Committees and had recently been appointed a medical member of the Area Health Authority. He was, at the time of his death, a member of the Welsh Manpower and Welsh Medical Committees. For three years he was Chairman of the Welsh Branch of The British Institute of Radiology as well as a member of the Council of The British Institute of Radiology. In recognition of his work he was awarded the Queen's Silver Jubilee Medal in 1977.

Hubert Jones was a Welsh rugby international, he had played for the Cardiff Rugby Club and had captained the Royal Navy Rugby XV. He was also a cricketer of county standard, having played for his native county of Glamorganshire.

Hubert was excellent company; he was an accomplished raconteur and exuded an infectious variety of humour and joviality. He will be sadly missed by his many friends and colleagues for his wise counsel, his unfailing loyalty and his diligence. During his latter years his activities in golf, fishing and gardening were curtailed by his numerous medical commitments.

Hubert is survived by his wife Rachel and their son Simon who is a doctor.

R.H.P.O.

Book reviews

Radiology of the Colon. (Ed. by J. R. Drayfuss and M. L. Janower), xxi+590 pp, 1980 (Williams and Wilkins, Baltimore), $66.00.
ISBN 0-683-02652-6

This book—Section 21 of Golden's Diagnostic Radiology Series—is edited by two staff members of the Massachusetts General Hospital. As one would expect, the book is comprehensive and well written, benefiting from the fact that the contributors have all at some period worked together. The student using this book in preparation for an examination will find that the text is clear and that the radiographs, which clearly demonstrate the pathological changes are of good quality, though it is a little surprising to find that many of the examples are of single-contrast barium type. A discussion of the methods of varying bowel preparation and the use of drugs such as glucagon is included. The chapter on the differential diagnosis which may arise in a case of colonic polyps is particularly useful. This book can be thoroughly recommended.

J. A. GLEESON.

Radiology of the Colon. By R. H. Marshak, A. E. Lindner and D. Maklansky. pp. xiii+788, 1980 (W. B. Saunders, Philadelphia). £34·25.
ISBN 0-7216-6219-7

This beautifully illustrated and detailed work is the long-awaited sequel to the authors' world-famous textbook on the radiology of the small bowel. In this magnificent book Marshak and his colleagues have invited contributions from a number of renowned radiologists. The whole is a superb text of some 22 chapters which range from that dealing with the anatomy and physiology of the large bowel to a miscellany containing, amongst other topics, descriptions of colitis cystica profunda and the colo-rectal problems of male homosexuals. The authors emphasise the need to consider both the clinical picture, the pathology and the changing radiological feature with chronicity. The radiographs are reproduced both clearly and accurately on good quality paper. A comprehensive list of references follows each chapter. Nothing has been overlooked and it is refreshing to note that there is a long and detailed chapter by Dr. Jack Rabinowitz on colonic disorders affecting infants and children. The authors are to be congratulated on producing a book of such excellence. At £34·25 it seems very reasonably priced and I feel sure it will soon grace the shelves of every departmental library.

J. PEMBERTON.

Pitfalls in Pediatric Chest Radiography. By H. White. pp. xi+136, 1980 (Harper and Row) £14·75.
ISBN 0-06-142682-2

This book is essentially an atlas and as the author says in his preface was written to "demonstrate an aid to the proper interpretation of chest radiographs in children". In the copy your reviewer received I am sorry to say that many of the illustrations were of an exceedingly poor quality. Even though accompanied by illustrative line diagrams, the radiographs were often still unintelligible. Some ten pages of introductory comments make some useful points but I cannot subscribe to the routine lateral view of the chest in children. I cannot recommend the purchase of this book with such poor illustrations as it, at present, contains. The biggest pitfall in paediatric radiology is not to have a decent radiograph.

D. G. SHAW.

Clark's Positioning in Radiography. 10th edition. Ed. by Louis Kreel, pp. 483, illus., 1979 (William Heinemann Medical Books, London), £22·50.
ISBN 0-433-18832-4

This volume is the latest edition of what has long been the standard textbook of radiography. It has commanded the affection as well as the respect of generations of radiographers and radiologists alike. This version has again been expanded to include brief references to the many additions to the science and art of radiography.

Unfortunately, the content and quality of this latest edition do not maintain the previous high standards. There are far too many factual errors which include wrongly-named carpal bones on p. 3, incorrect references to illustrations and variations in terminology between the script and the diagrams. Some of the text has not survived the repeated amendments and parts are now quite unintelligible. Some of the original illustrations are showing their age and some of the new do not reveal the detail the radiographer would seek to produce: one picture of the hips has been printed upside down. In all, the book evokes more nostalgia than interest, highlighted by the retention of a section on kymography, while too many useful projections have been omitted.

Perhaps it is time for the various sections to be allocated to pairs of radiology and radiography experts who should be asked to provide a "New Testament". Dare it be said that the "Old Testament" is in danger of falling from grace?

J. ROYLANCE,
M. HARRISON.

Self-Assessment of Current Knowledge in Diagnostic Radiology. Ed. T. Keats, 2nd edition, pp. 256, 1980 (Medical Examination Publishing Co., New York), £16·50.
ISBN 0-87488-278-8

In his Preface to this book, Dr. Keats reminds us that continuing competency of medical practitioners is increasingly demanded by the medical profession and by the public. With this in mind, he has enlisted the services of 16 colleagues from the University of Virginia School of Medicine, each of whom has produced a section of multiple choice questions. Each body system is covered and there are separate sections on body computerized tomography, mammography, ultrasound and special procedures in radiology. Many of the questions demand an understanding of radiographic appearances but there are also many which expect the reader to be orientated along diagnostic clinical pathways. Each question is backed up by a reference from the acceptably current literature.

I was dismayed by my own performance—particularly in those sections in which I have a particular interest! After talking with my colleagues I have a sneaking suspicion that I am not unique in this respect. I was heartened to read that such ignorance may itself induce retention of the correct information the "next time round". This book will not appeal to a number of people but I suspect that it will be of interest to a good many more. By its very nature it is rather an indigestible text and needs to be taken in small portions when the mood is right. It is a small inexpensive paperback which may frighten Senior Registrars preparing for the F.R.C.R. but which should be looked at by their mentors.

C. D. R. FLOWER.

Book reviews

The Physics of Medical Imaging: Recording System Measurements and Techniques. Ed. by Arthur G. Haus, pp. 613, 1979 (American Institute of Physics, Inc., New York), $35.00.
ISBN 0-397-50428-4

In July 1979 the American Association of Physicists in Medicine ran a summer school on The Physics of Medical Imaging: Recording System Measurements and Techniques. Each participant received a book with typescripts of 34 papers to be presented to the course, and these, together with the discussions at the ends of the six sessions, have been edited to form the book.

The aim stated in the preface is to present the medical physicist with "information on medical imaging systems in terms of their basic characteristics, correct and established methods and measurements for evaluation, and selection and use for various diagnostic imaging procedures".

Thirty-one contributors are listed, representing universities, industry and the Bureau of Radiological Health, so it is not surprising that there are differences in style, and even in type face, between the papers.

The six main sections cover the screen-film system, image intensifiers, electrostatic systems, diagnostic imaging techniques, image evaluation and a single section covering computed tomography, ultrasound and nuclear medicine. The papers vary from a detailed and mathematical analysis of some subjects, such as xeromammography, to a rather superficial comparison of computed tomography, ultrasound and nuclear medicine. There are numerous clear line drawings, but some of the half-tone illustrations are rather poor, particularly those that appear to have been recorded on Polaroid. Few people praise Polaroid but many use it, and some medical imaging equipment is sold with a cathode-ray tube and Polaroid camera as the standard hard copy device. It is a pity that a book which deals in great detail with conventional film should mention the use of Polaroid only briefly in a discussion. Computerized tomography scans and many gamma-camera and ultrasound images are stored in computer memory, so a discussion of hard copy devices other than cathode-ray tube and camera would have increased the value of the book.

There is a lot of useful information in this book, but it has no index and the table of contents gives only the titles and authors of the papers; it cannot therefore be recommended as a reference manual. As a series of review articles covering a wide range of topics in medical imaging it could be of interest to many physicists and engineers working in medical imaging.

J. C. W. Crawley.

Essential Physics for Radiographers. By J. L. Ball and A. D. Moore, pp. xi+252, 1980 (Blackwell Scientific Publications, Oxford), £6·50.
ISBN 0-632-00644-7

Rarely can a text book claim to be readable and comprehensive. This book, written by J. L. Ball and A. D. Moore, is divided into twenty chapters which corresponds to the physics course lectures at the South West Wales School of Radiography and is intended for Part I examination of physics for the Diploma of The College of Radiographers.

The opening chapter relates to general physics, matter, energy, measurement and units, as well as physical quantities. So easy reading is the chapter, it is with delight that one tackles the problem section, for example, "What force would be required to accelerate a stretcher trolley at 1 m/s^2 if its mass is 20 kg and carries a patient of 80 kg?" The book then consists of a further 19 chapters, each covering a concept of physics in a similar fashion.

The chapter summaries are most useful, giving definitions of key words and formulae.

The chapter on rectification was found to be of particular interest, relating to the principals of semi-conductors, fusing of p-type with n-types forming depletion zones which may be reduced in the presence of an external battery. Individual chapters may be criticized for brevity; in particular those on thermionic emission and the stationary anode X-ray tube, though perhaps in a text book of this kind this is reasonable.

However, this book, written by radiographers for radiographers, must be useful reading material for all potential physics candidates.

J. R. L. Nettle.

Information Processing in Medical Imaging 1980. Proceedings of the Sixth International Conference, Paris July 2-6 1979. (INSERM, Paris), 120 Fr.
ISBN 2-85598-191-3

This publication presents a comprehensive collection of current research studies mainly in the field of nuclear medicine, but also contains, for variety and good measure, X-ray, ultrasound and nuclear magnetic resonance imaging studies to illustrate the interaction between these imaging modalities. The reproduction of the papers, both text and figures, is of adequate quality and there are brief accounts of probing and informative discussions.

The nuclear medicine papers account for two-thirds of the total. Physics and engineering aspects of the instrumentation include the high-purity germanium gamma camera, ways of correcting non-linearity and non-uniformity in Anger and image intensifier gamma cameras, and papers on emission tomography systems. Dynamic function studies of considerable complexity are described which illustrate the computing effort currently being applied and the state of the art. There are also papers on display systems, ROC curves and the general layout of small computer networks which should be of interest to more than the nuclear medicine enthusiast.

The remaining one-third of papers include processing of coronary angiograms, quantitative aspects of X-ray computed tomography, ultrasound, NMR and proton radiography.

In a brief review of this book it is almost impossible to summarize results. Many of the authors openly admit that the new techniques still require validation clinically, but information processing is continually developing. By incorporating more and more "*a priori*" knowledge and human experience into the software, more intelligent hardware should be forthcoming.

The organizers of the Conference and the Scientific Committee deserve praise for covering such a broad spectrum of topics of current interest, as do the individual contributors for the scientific content of their papers. There is something for everyone with an interest in the medical applications of image processing—clinician, physicist, systems analyst and everyone should have a look. The papers are in English (with the exception of one in French) with summaries in French.

W. I. Keyes.

Book reviews

The radiology of tuberculosis 116
Cerebral aneurysms 121
Advances in neurosurgery. 7 121
Correlative sectional anatomy of the head and neck 121
Atlas of computerized emission tomography 125
Handbuch der medizinischen Radiogie. XIII, 2 131
Radiation oncology—rationale, technique, results 131
Radiation therapy technology examination review 135
La xeromammografia 167
Das Röntgenbild 173
Illustrated guide to X-ray technics 173
Radiology of the colon (Golden's Diagnostic Radiology 21) 177
Radiology of the colon 177
Pitfalls in pediatric chest radiography 177
Clark's positioning in radiography 177
Self-assessment of current knowledge in diagnostic radiology 177
The physics of medical imaging 178
Essential physics for radiographers 178
Information processing in medical imaging 178
Books received 148

High dose-rate after-loading in the treatment of cancer of the uterus

Edited by Thelma D. Bates and Roger J. Berry

British Journal of Radiology Special Report 17

For more than fifty years intracavitary irradiation has formed a major part of the treatment of cancer of the cervix and corpus uteri. In recent years high dose-rate remote after-loading devices have been developed which have removed all radiation hazards to medical and ancillary staff and other patients, but until now the question "Are the clinical results achieved by high dose-rate after-loading intracavitary treatment of carcinoma of the cervix and corpus uteri at least as good as those achievable by conventional low dose-rate intracavitary techniques?" had not been answered by adequate clinical experience. At a meeting held at The Middlesex Hospital Medical School, London from 10–12 April 1978, 86 participants and observers from 36 Hospital Centres in 15 countries gathered to discuss relevant physics and radiobiology studies and to pool their clinical experience in the use of high dose-rate after-loading devices. This volume presents brief versions of their 33 contributed papers and a distillation of the lively discussion which took place. Although the conclusions reached were necessarily cautious, lest future results not reflect those already achieved, those so far with remote high dose-rate after-loading appear to be in no way inferior to the results of traditional methods. In fact there are indications that high-dose fractionated intracavitary therapy may be associated with a lower incidence of normal tissue complications for a comparable level of achievement of tumour local control in cancer of the cervix and corpus uteri.

High dose-rate remote after-loading devices have the ability to treat very large numbers of patients, and have a particularly valuable contribution to make in the treatment of these distressingly common cancers in developing countries. This volume provides a comprehensive view of clinical and radiobiological experience for those centres acquiring or considering high dose-rate after-loading equipment.

Orders to: Price **£15**
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
(01–935 6237) or through your bookseller.
ISSN: 0306–2120
ISBN: 0–905749–07–3

VOL 54 NO 638 **FEBRUARY 1981**

The British Journal of Radiology

Contents

Page

Positron-emitting radionuclides in the study of metabolic and physiopathologic mechanisms. 91
Mackenzie Davidson Memorial Lecture, April 1980.
C. Kellershohn

The radiology of carcinoma of the ear. 103
P. D. Phelps and G. A. S. Lloyd

Krypton 81m ventilation scanning in chronic obstructive airways disease. 110
D. A. Cunningham and J. P. Lavender

A longitudinal study of the growth of the nasopharynx and its contents in normal children. 117
W. D. Jeans, D. C. J. Fernando, A. R. Maw and B. C. Leighton

Recognition of the superscan in prostatic bone scintigraphy. 122
A. R. Constable and R. W. Cranage

Mediastinal lymphoscintigraphy in ovarian cancer using intraperitoneal autologous technetium-99m-labelled erythrocytes. 126
W. D. Kaplan, W. D. Bloomer, A. G. Jones, J. Federschneider and R. C. Knapp

Different fractionation schemes tested by histological examination of autopsy specimens from lung cancer patients. 132
H. J. Eichhorn

Scientific note. 136
Brachytherapy build-up factors.
R. O. Kornelson and M. E. J. Young

Technical note. 137
Protective effect of spectacles.
M. J. Day and E. Forster

Case reports. 139
Transgression of localizing wire into the pleural cavity prior to mammography.
J. B. Bristol and P. A. Jones
Upward dislocation of the first rib: a rare cause of nerve entrapment producing brachialgia.
C. C. McCormick, S. S. Gubbay and J. S. Lekias
A fibrovascular polyp of the oesophagus.
Y. Barki, H. Elias, F. Tovi and J. Bar-Ziv
Lymphoma of the colon detected by CT.
J. Hildell, U. Nyman and J. -E. Rosengren
Unusual ophthalmic metastasis from a bronchial carcinoma.
S. Scavdis, G. Tritakis and G. Ramantanis

Short communications. 149
Human whole-body NMR tomographic imaging: normal sections.
W. A. Edelstein, J. M. S. Hutchison, F. W. Smith, J. Mallard, G. Johnson and T. W. Redpath
Whole-body tomographic imaging by NMR.
V. Bangert, P. Mansfield and R. E. Coupland
Teratogenic and radiosensitizing effects of misonidazole on mouse embryos.
C. Michel and H. Fritz-Niggli

Correspondence. 156
Neurotoxicity with desmethylmisonidazole.
S. Dische, M. I. Saunders and M. R. L. Stratford
Contrast media for hysterosalpingography.
N. Caporn, S. Gilani and W. D. Jeans
X-ray tube lifetimes with the Leeds General Infirmary EMI brain scanner.
P. C. Shrimpton and D. W. Dewhirst

Proceedings of Symposium Mammographicum 80. 159

Proceedings of The British Institute of Radiology. 168
Symposium in honour of Dr. Frank Ellis.
Silverless X-ray imaging

Forthcoming events and notices. 174

Obituary: Dr. H. E. Jones 176

Printed in Great Britain by Lund Humphries
London and Bradford
Published by The British Institute of Radiology
32 Welbeck Street, London W1M 7PG

ISSN 0007–1285
16180

14.9.81

Volume 54 Number 63
March 198

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis

Radiation [illegible]

Nuclear [illegible]

[illegible]

[illegible]

[illegible]

[illegible]

and [illegible]

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01–935 6237 and 01–935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

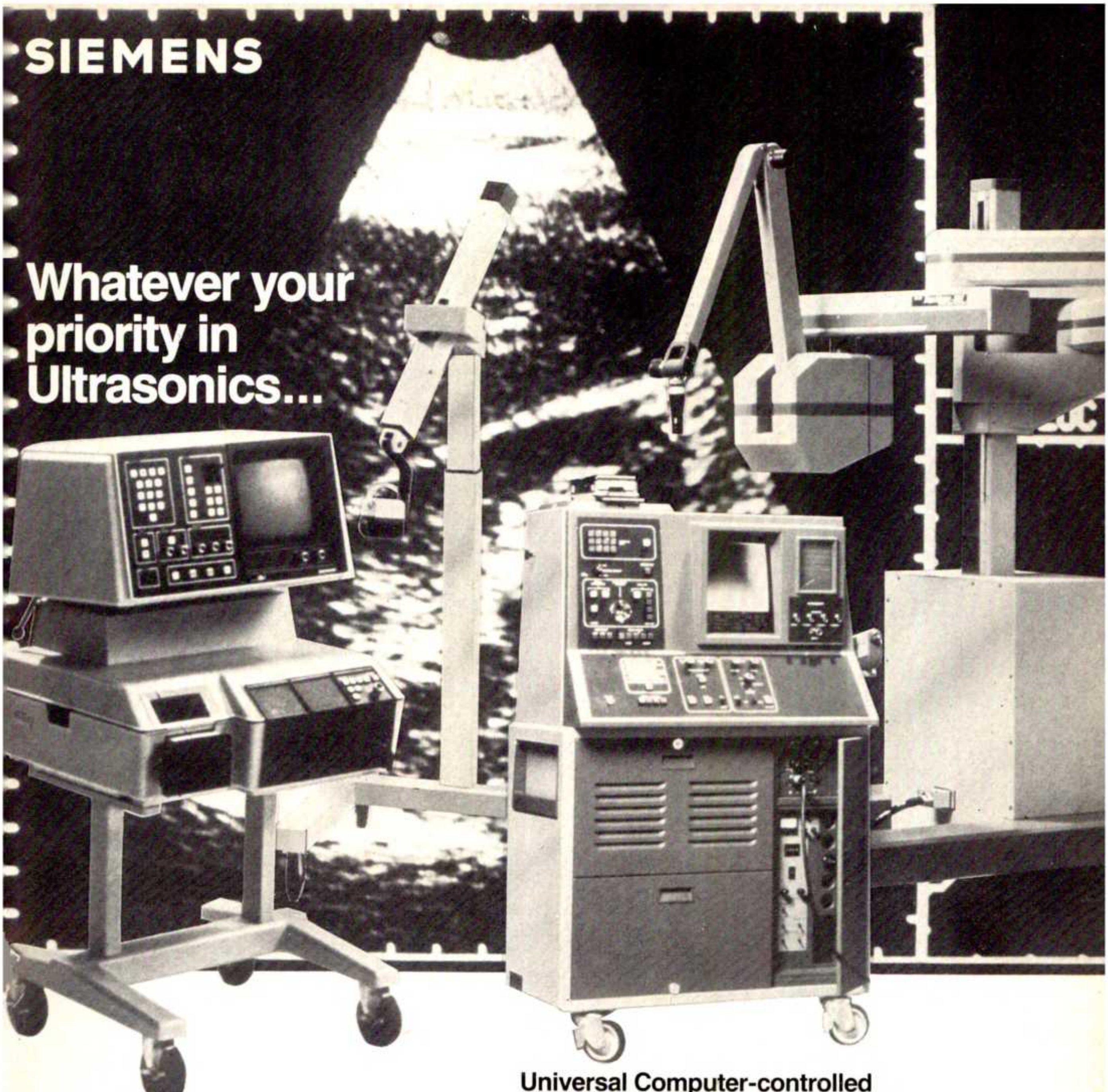
Hon. Secretaries

M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981



SIEMENS

Whatever your priority in Ultrasonics...

Automatic, Computer-controlled Dynamic and High Resolution Static B-scanning

The Sonography System RA-1 diagnostic ultra-sound scanner uses sophisticated, computer-controlled image processing to achieve superior image resolution. The advanced, state-of-the-art scanheads comprise:

❊ LFOV scanheads for multiformat abdominal scanning.
❊ WV scanheads for high frame-rate scanning.
❊ Small parts scanhead, incorporating Doppler with Spectral Analysis, for superficial vessel and organ studies, for neonatal and paediatric scanning.

The modular design guards against obsolescence whilst permitting expansion and the ability to retrofit new imaging techniques as they are developed.

Universal Computer-controlled High Resolution Static B-scanning

The Universal Pho/sonic-SM fully-integrated computer-controlled, high performance ultrasound scanner which produces excellent image resolution. It is designed to meet individual requirements through a variety of system options, including:

❊ Wide range of transducers ❊ Image Process Functions
❊ Area, Circumference and Volume measurements.
❊ Obstetrics measurement facility ❊ Floppy disc interface

Future improvements to the image processing may be incorporated due to the flexible computer software.

Other Siemens ultrasound equipment is available, including the IMAGER 2300, a Dynamically Focused Linear Array Real-Time B-scanner. For full details write to: Siemens Medical Group, Siemens Limited, Windmill Road, Sunbury-on-Thames, Middlesex TW14 7HS. Telephone Sunbury (09327) 85691.

...Siemens gives you the choice!

UNIVERSITY OF RIYADH
COLLEGE OF ALLIED MEDICAL SCIENCES
RIYADH, SAUDI ARABIA

Faculty and technical staff positions are available in the following programs beginning the 1981–82 academic year:

Diagnostic Imaging
Radiation Therapy
Sonography
Health Education
Health Services Administration
Medical Records
Dietetics
Environmental Health
Clinical Laboratory Sciences
Physical Therapy
Orthotics/Prosthetics
Respiratory Therapy
Occupational Therapy
Biomedical Instrumentation
Ophthalmic Technology
Nursing
Continuing Education
Audio-Visual Technology

Responsibilities will include teaching in Bachelors degree programs and continuing education courses, as well as assisting in the overall development of the newly established college. Benefits include: generous salary; accommodation or accommodation allowance; paid vacation; round trip to place of origin once a year including family; and an end of service bonus.

Applications will be held in strict confidence. Interviews will take place in the U.S.A. and the U.K. during June/July 1981. Other interviews may be conducted later for those who wish to join after the commencement of the academic year.

Interested applicants should write to the address below for application forms:

Dean,
College of Allied Medical Sciences,
University of Riyadh, P.O. Box 10219, Riyadh, Saudi Arabia
Tel. No.: 435–6644. Telex No.: 201019R UNIV SJ.

Clinical and Experimental Applications of Krypton 81m

Edited by J. P. Lavender

British Journal of Radiology, Special Report 15.
This work is composed of papers presented at an International Meeting held in June 1977 concerned with a new physiological tool; the use of a very short-lived radioactive gas krypton 81m.
Krypton 81m is a noble gas with a 13 second half life available from a portable generator with a half life of 4½ hours. Although known for a number of years it has only been used with any frequency by physiologists and clinicians since 1975.
The first section of the book deals with the production of the parent isotope rubidium 81 and the design of generators. The second section comprises a series of papers concerned with the use of the equilibrium image as both a picture and a measure of regional lung ventilation and perfusion. It also outlines problems of deriving absolute values of lung function. In the third section, papers illustrate the use of krypton 81m as a clinical tool in the diagnosis of pulmonary embolic disease and other pulmonary diseases and compare such information with that obtained from the more familiar xenon 133. In the last section the use of intra-arterial krypton as a marker of regional myocardial and cerebral blood flow is discussed. This technique, which has been most highly developed in the case of the myocardium, allows detailed images of the myocardial perfusion to be recorded. Perhaps its clearest application is in following rapid changes of regional myocardial perfusion in response to transient ischaemia, stress and drugs.
The discussion following each paper allows an assessment of the value and place of this new technique.

ISBN 0 905749 01 4
ISSN 0306–2120
Price **£12**
Orders to:
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237) or through your bookseller.

PRM 80

The T.E.M. programmed radiotherapy microcomputer has been developed to handle the everyday task of accurately calculating a patient's treatment dose and/or time.

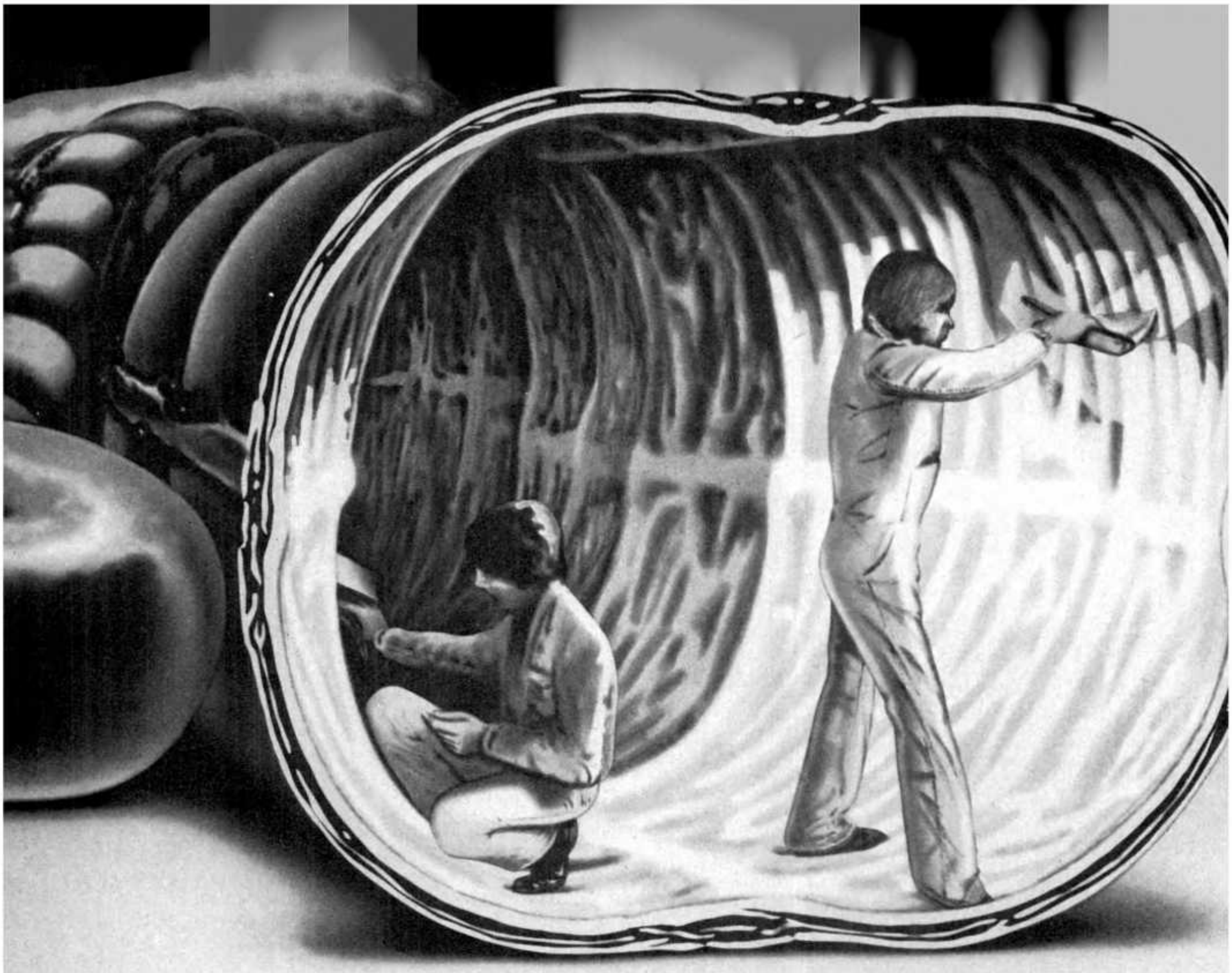
From these entries:	The PRM 80 gives:
Field sizes	Treatment Time
S.S.D.	Set Dose
Attentuation Factors	Skin Dose.
Depth of Tumour	
Prescribed Dose Etc.	

Capable of calculating opposed field and off-axis data, the PRM 80 also has an optional facility giving the total number of treatments, cumulative dose and the ret dose.

The PRM 80 prints out all this data, including the actual treatment time which is recorded from its own internal timer.

TEM

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England
Tel: 0293 31244 Telex: 87397, Grams: TESTMENT CRAWLEY



baritop ensures smooth and even coating of the GI tract

The high density, low viscosity and ultra-fine particle size of Baritop allows optimum visualisation of the areae gastricae and the innominate grooves. Baritop consistently gives excellent resolution.

Baritop 100 is a ready made suspension supplied in a ring-pull can for easy use. If you prefer a higher density use Baritop G powder.

Baritop makes the most of your double contrast technique.

Concept Pharmaceuticals Ltd.,
Russell House, 59-61 High Street, Rickmansworth WD3 1EZ
Tel: Rickmansworth (092 37) 79388/9/0 Telex: 925794

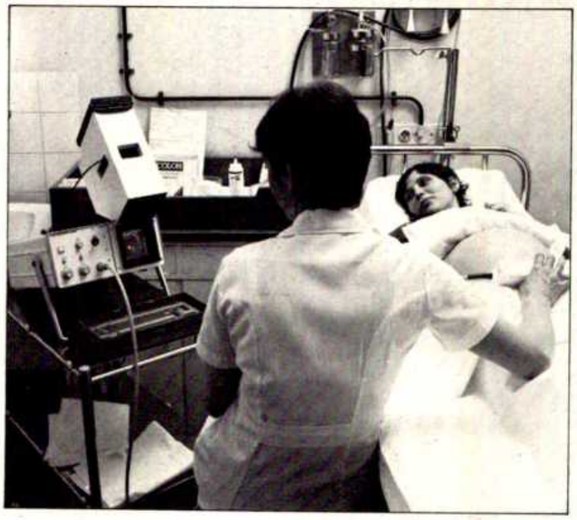
baritop

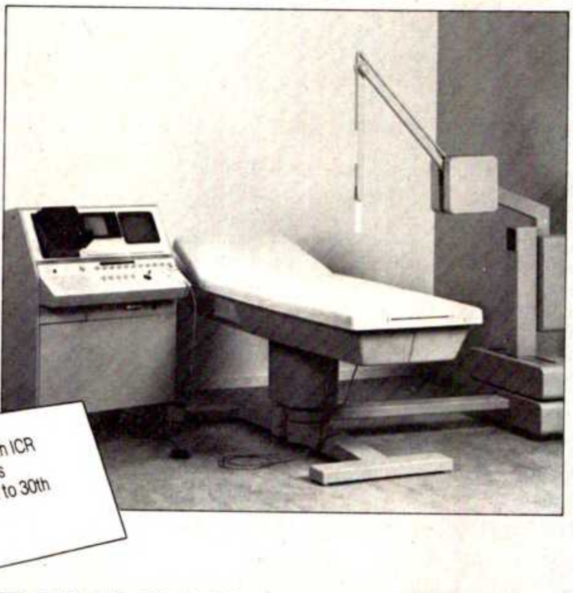
for those who seek perfection

IT'S YOUR RESULTS THAT MATTER.

In ultrasound diagnosis.

Since today ultrasound is firmly established as a first order diagnostic method, more attention is concentrated on image quality and application flexibility. Anticipating this, we developed a range of ultrasonic systems to ensure a high standard of diagnostic confidence.
To achieve superior image quality we employed new techniques and digital pre- and post-processing including digital scan conversion. Special transducers such as the new servo sector ensure clear signal input.
You can see the difference. And you can select a system perfectly adapted to your diagnostic needs.
This applies to the truly portable (8.8 kg) real-time Sono DIAGNOST R1000 that permits examinations where and when needed without delay.
It applies as well to the universal self-contained scanning systems of the Sono DIAGNOST B7000 series, covering the entire spectrum of ultrasonic examination and diagnosis. They comprise A-mode, B-scan, M-mode and real-time. These systems are truly modular and can easily be adapted to your special requirements.
The compact console is ergonomically designed for effortless operation. A wide choice of scanning arms, transducers and examination tables corresponds with clinical requirements.
Many special features such as the unique hand controller facilitate and speed the examinations.
When you work with one of these systems and see how fast and efficiently diagnostic results are obtained you know what we mean by a high standard of diagnostic confidence.
To get full details about the Sono DIAGNOST systems please mail the coupon.*
Philips Medical Systems cover the range of advanced diagnostic imaging and radiation therapy.





See us at the 15th ICR
at Brussels
from June 24th to 30th
1981.

PHILIPS

Medical Systems

* UK enquiries: Philips Medical Systems, Kelvin House
63/75 Glenthorne Road, Hammersmith, London W6 OLJ.

I want INFORMATION about
Sono DIAGNOST systems

me
pital
et
n
ntry

Philips Industries
ical Systems Division
eting Communica
Eindhove
erland

THE ONTARIO CANCER FOUNDATION
TORONTO-BAYVIEW CLINIC

Radiation Oncologists

Radiation Oncologists are required for this new cancer centre which is associated with Sunnybrook Medical Centre and the University of Toronto. Construction of the out-patient and radiation treatment facility will be completed in September 1981. There will be an associated in-patient oncology unit of 85 beds in Sunnybrook Hospital. An interim centre is currently operational.

The Centre will treat 2500 new patients a year and will have a major research orientation. The initial staff will include six Radiation Oncologists, six Medical Oncologists and three Physicists. The radiation equipment will include two 25 MEV and one 6 MEV linear accelerator and a cobalt unit.

Radiation Oncologists will be responsible for the total care of patients treated with radiation, whether as in-patients or out-patients.

Applicants should indicate their research interests which will be an important consideration with these appointments.

Interested individuals should send a curriculum vitae and the names of three referees to: **Dr. R. D. T. Jenkin, Director, The Ontario Cancer Foundation, Toronto-Bayview Clinic, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5.**

Lennox and Addington County General Hospital, Napanee, Ontario, Canada

Radiologist

Applications are invited from suitably qualified Specialists to serve as Radiologist to this 66-bed full accredited active general hospital.

The Active Medical Staff includes 11 Family Physicians, an Internist and a General Surgeon.

The Hospital serves a County with a population of approximately 30,000, and the Radiologist carries out approximately 2,500 inpatient and 12,000 outpatient examinations per annum.

Napanee is a small town located in Eastern Ontario – 25 miles West of Kingston, home of Queen's University and associated Tertiary Care Medical Centre.

The position is available as of March 1st, 1981.

The applicant must be eligible for registration in the Province of Ontario.

Please submit résumé, credentials and references to:

W. A. Ronald, Administrator
Lennox and Addington County General Hospital
8 Park Drive
Napanee, Ontario, CANADA K7R 2Z4

Computers in the Control of Treatment Units

The British Institute of Radiology: Special Report No 16, March 1979

by R. E. Bentley, A. L. Bradshaw, C. A. F. Joslin, W. J. Redmond, M. E. Rosenbloom, B. J. Scholl-Evans, J. B. H. Stedeford and R. C. Tudway.

Digital computers are being used very successfully in radiotherapy dose computation. This report deals with another, at present less highly developed, application of computers, the provision of some degree of automation at the point of treatment. Drawing on their own practical experience, on information from manufacturers and on the relatively sparse literature on this topic, the authors analyse the reasons for wishing to introduce some automation, discuss suitable techniques and procedures and make specific recommendations. Practical problems in implementing such control systems, including the need to gain acceptance from those operating the equipment and from those being treated, are carefully considered.

The authors were of a multidisciplinary Task Group, convened by Dr. Roy Bentley, which had been set up by the British Institute of Radiology Working Party on "Applications of Modern Technology in Radiotherapy."

The report should be of interest to all those concerned as users, designers or manufacturers with future developments of radiotherapy apparatus.

Orders to:
The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG

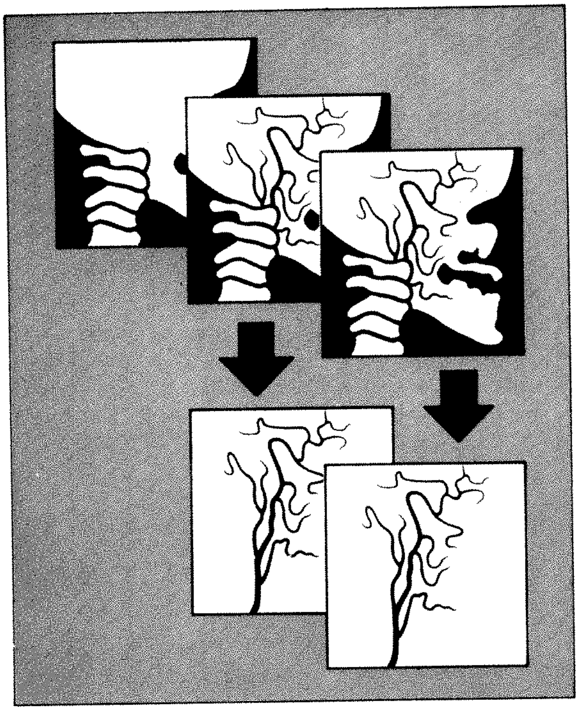
or through your bookseller Price: £2·40

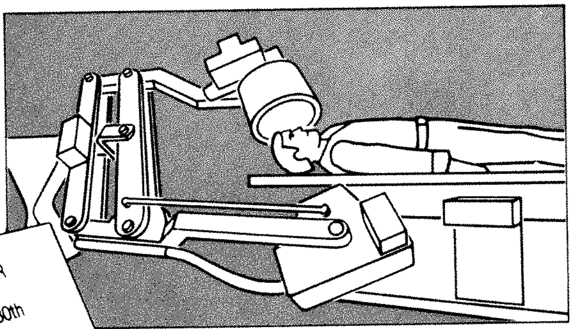
ISSN 0306–2120
ISBN 0–905749–04–9

IT'S YOUR RESULTS THAT MATTER.

Digital vascular imaging.

Angiography on out-patients? No more aggressive than routine IV urography? Completely processed and subtracted images in real-time?
It is being practiced successfully already.
We have achieved another breakthrough in angiography by utilizing advanced digital technology.
Philips Digital Vascular Imaging (DVI) is an electronic processing system which permits intravenous angiography with real-time image subtraction in three modes and off-line post processing in the fourth mode. You can select serial or continuous imaging or the time interval difference mode (TID). Post processing recalls images stored on video tape or video disc.
The system gives every indication of becoming the first order diagnostic modality for most vascular examinations – not only for asymptomatic and high risk patients. It can easily be integrated in all Philips angiographic systems.
Digital Vascular Imaging is a natural complement to Philips "total systems" approach to angiography. From the proven line of Poly DIAGNOST X-ray stands and patient support devices to imaging systems, generators and X-ray tubes.
To get full information about Philips Digital Vascular Imaging and the new angiographic system please mail the coupon. *
Philips Medical Systems cover the range of advanced diagnostic imaging and radiation therapy.





See us at the 15th ICR
at Brussels
from June 24th to 30th
1981.

PHILIPS Medical Systems

* UK enquiries: Philips Medical Systems, Kelvin House
63/75 Glenthorne Road, Hammersmith, London W6 OLJ.

I want INFORMATION about
○ Philips DVI ○ Poly DIAGNOST A/Angio DIAGNOST 2
Name
Hospital
Street
Town
Country

Philips Industries
Medical Systems Division-QM.
Marketing Communications
Detp., Eindhoven, the
Netherlands BJR.

THE FACULTY OF
RADIOLOGISTS
OF
THE ROYAL COLLEGE
OF SURGEONS IN IRELAND

**21st
ANNIVERSARY
MEETING**

to be held in

**DUBLIN
2nd-3rd OCTOBER 1981**

with

THE BRITISH INSTITUTE OF
RADIOLOGISTS
ROYAL COLLEGE OF
RADIOLOGISTS
ROYAL SOCIETY OF MEDICINE

Diagnostic and Therapy Sessions

Topics to include
Radiology in Renal Failure
Radiology of Trauma

Proffered Papers
BIR Presidential Address:
Dr. David Trapnell
"Chest Radiology–Guesswork or
Science"

Technical Exhibition

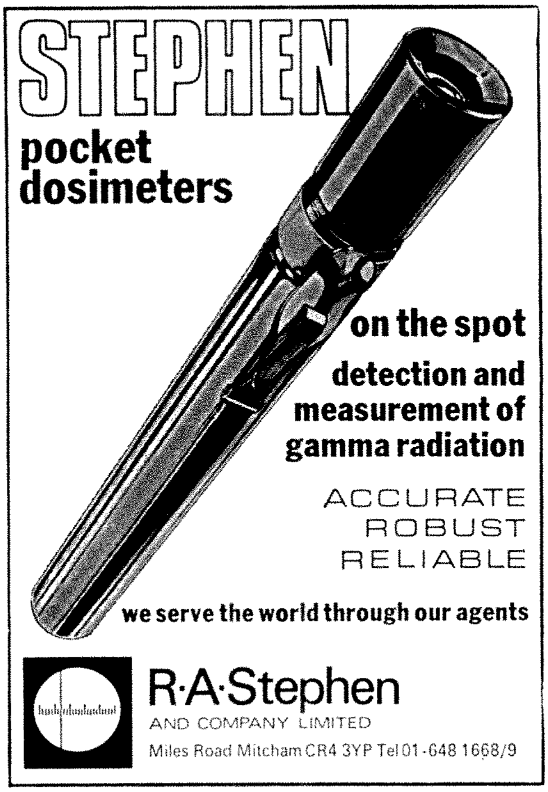
Further information from
Miss Anne Daly,
Faculty of Radiologists,
Royal College of Surgeons in Ireland,
Stephen's Green, Dublin 2

Neuroradiologist

Full range of diagnostic and interventional activities. Excellent research facilities. Teaching, research and patient care responsibilities. Salary range $50,000–$75,000 depending upon experience and faculty rank. Contact M. S. Lapayowker, M.D., Department of Diagnostic Radiology, Temple University Hospital, Philadelphia, Pa. 19140, U.S.A.

Vascular Radiologist

Full range of diagnostic and interventional activities. Excellent research facilities. Teaching, research and patient care responsibilities. Salary range $50,000–$60,000 depending upon experience and faculty rank. Contact M. S. Lapayowker, M.D., Department of Diagnostic Radiology, Temple University Hospital, Philadelphia, Pa. 19140, U.S.A.



R·A·Stephen
AND COMPANY LIMITED
Miles Road Mitcham CR4 3YP Tel 01-648 1668/9

A system for the 80s that's sure to please……………

Ceiling Tube Support CH-30X

Features

- Light movement
- Safety
- Convenient, simple operation

The XS-10 features the ease of operation, safety and reliability that only 100 years of SHIMADZU experience in medical engineering can offer.

90°/90° UNIVERSAL DIAGNOSTIC TABLE XS-10

- 90°/90° table tilting
- Automatic field collimation
- Exposure program up to 14" × 14" (35 cm × 35 cm)
- Cassette loading from either side of spot film device
- Reciprocating X-ray grid in spotfilming
- Built-in bucky device
- 7" image amplifier attachable without ceiling suspension

See SHIMADZU at the ICR-81, Brussels, June, 1981
Booth No. 9203 & 9302

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160
Japan Phone: Tokyo 03-346-5461 Overseas Telex No 0232-3291 SHMDT J
Cable Address: SHIMADZU TOKYO
SHIMADZU (EUROPA) GmbH
4000 Dusseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D

Carcinogenesis and Radiation Risks: a Biomathematical Reconnaissance

by W. V. Mayneord, C.B.E., D.Sc., F.R.S. and R. H. Clarke, Ph.D.

with foreword by Sir Eric Pochin, M.D.

British Journal of Radiology Supplement No. 12, 1975; reprinted 1979.

The first printing of this refreshingly original monograph by Professor Mayneord and Dr. Clarke was sold out. In view of the increasing interest in the topics dealt with by the authors, the work was reprinted. It explores some of the fundamental problems that arise when one attempts to predict the biological effects of a given dose of radiation. The authors point out that, in attempting an estimate of biological effect, for example carcinogenesis, it is frequently assumed that the risk is simply proportional to the dose received, although biological experiment often reveals a much more complex relation between effect and dose. They examine some of the consequences of taking such complex relationships into account in assessing "risk" on the basis of "dose" and propose a formula relating the risk to a whole population of cells from a rare event, such as the "transformation" of a single cell or group of cells. The parameters of the basic formula can be varied to meet particular assumptions regarding the distribution of dose in tissue and of response to dose. Using this formula, analyses are made of many different types of problem, including those presented by "point sources". It is emphasized throughout that the derivation of probabilities is not merely an exercise in mathematical physics but also involves cytology, genetics, immunology and hormone physiology, as well as studies of viral and chemical carcinogenesis. However, the method of analysis used leads to a clearer definition of the problems that have to be studied in attempting to produce more logical estimates of the risks from radiation, and the quantities of significance in designing experimental investigations.

The monograph represents a detailed development of ideas presented by Professor Mayneord in his Mackenzie Davidson Memorial Lecture of 1968 on "Radiation Carcinogenesis" and workers in the fields of radiobiology, experimental carcinogenesis and health physics will gain valuable insights from this study.

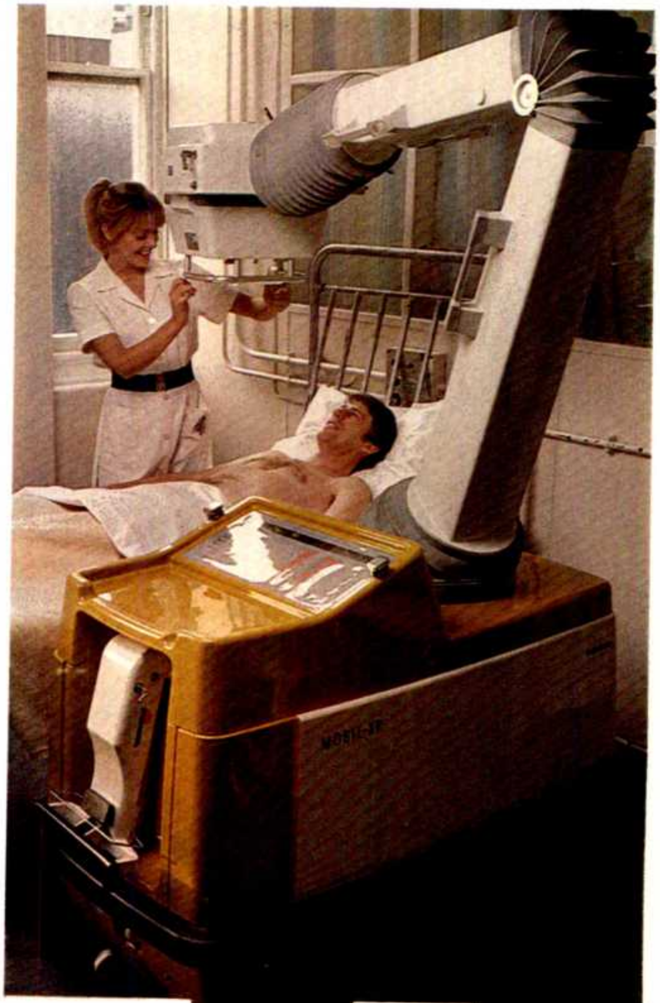
Orders to : Price **£6·50**
Publications Department, The British Institute of Radiology,
32 Welbeck Street, London, W1M 7PG (01–935–6237) or your bookseller.

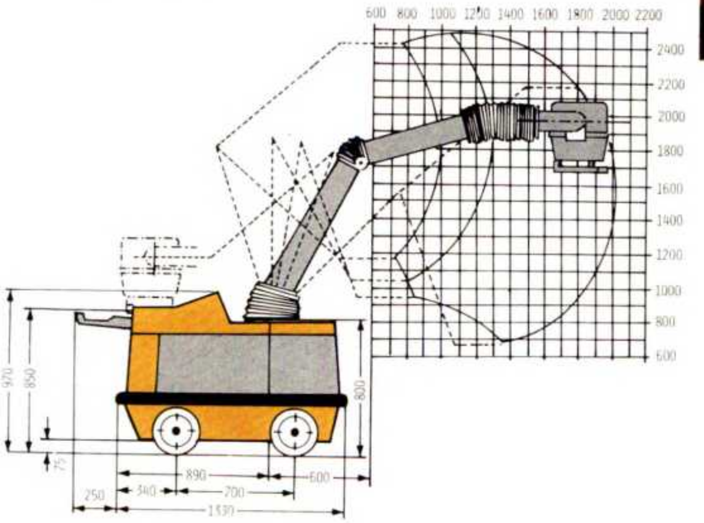
SIEMENS

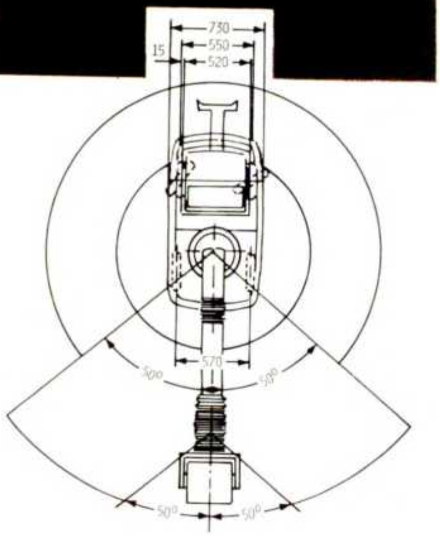
Mobil XR – brings a microprocessor controlled, aseptic mobile radiography unit to the patient.

The battery-powered MOBIL XR is self-propelled and self-contained with microprocessor controls providing full power exposures at 20 kW time after time. The adjustable counter-balance arm and a wide range of alphanumerically displayed exposure parameters allow sharp image examination of any organ or limb. Aseptic design with touch controls and total enclosure fo all components make it ideal for theatre use. Infinitely variable speed control makes it easy to manoeuvre and pull-out cable allows simple recharging at any power point.

For further details or a demonstration contact:
Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS.
Tel. Sunbury (09327) 85691.







In the world of mobile radiography Siemens has the answer.

بسم الله الرحمن الرحيم

Kuwait Oil Company
(K.S.C.)

شركة نفط الكويت
(ش.م.ك.)

Applications are invited for the post of

Consultant Radiologists

to work in well-equipped hospitals
including C.T. Scanners and Ultrasonography.

Applicants must have F.R.C.R.

Salary 800–850 K.D. (1 K.D. approximately = £1·54) tax free.

Free furnished accommodation supplied.

Apply to: **Dr. Na'il Al-Naqeeb, F.R.C.S.Ed., Under Secretary,**
Ministry of Public Health, Kuwait, P.O. Box 5.

High dose-rate after-loading in the treatment of cancer of the uterus

Edited by Thelma D. Bates and Roger J. Berry

British Journal of Radiology Special Report 17

For more than fifty years intracavitary irradiation has formed a major part of the treatment of cancer of the cervix and corpus uteri. In recent years high dose-rate remote after-loading devices have been developed which have removed all radiation hazards to medical and ancillary staff and other patients, but until now the question "Are the clinical results achieved by high dose-rate after-loading intracavitary treatment of carcinoma of the cervix and corpus uteri at least as good as those achievable by conventional low dose-rate intracavitary techniques?" had not been answered by adequate clinical experience. At a meeting held at The Middlesex Hospital Medical School, London from 10–12 April 1978, 86 participants and observers from 36 Hospital Centres in 15 countries gathered to discuss relevant physics and radiobiology studies and to pool their clinical experience in the use of high dose-rate after-loading devices. This volume presents brief versions of their 33 contributed papers and a distillation of the lively discussion which took place. Although the conclusions reached were necessarily cautious, lest future results not reflect those already achieved, those so far with remote high dose-rate after-loading appear to be in no way inferior to the results of traditional methods. In fact there are indications that high-dose fractionated intracavitary therapy may be associated with a lower incidence of normal tissue complications for a comparable level of achievement of tumour local control in cancer of the cervix and corpus uteri.

High dose-rate remote after-loading devices have the ability to treat very large numbers of patients, and have a particularly valuable contribution to make in the treatment of these distressingly common cancers in developing countries. This volume provides comprehensive views of clinical and radiobiological experience for those centres acquiring or considering high dose-rate after-loading equipment.

ISSN: 0306–2120
ISBN: 0–905749–07–3

Price **£15**

Orders to:
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
(01–935 6237) or through your bookseller.

GEVAERT AGFA-GEVAERT

These products are now available from Agfa-Gevaert

ILFORD X-RAY FILM

RAPID R TYPE S
RAPID R
ILFEX 90
ILFOSCAN/ILFOSOUND

Please order from one of the following offices

LONDON & SOUTH
French's Avenue, Dunstable, Beds.
Telephone: 0582 64101

NORTH & NORTH WALES
43 North Street, Cheetham, Manchester 8
Telephone: 061-833 9321

SCOTLAND
41 Watson Crescent, Edinburgh 11
Telephone: 031-337 7337

NORTHERN IRELAND
4 Crescent Gardens, Belfast 7
Telephone: 0232 43693

APPEAL

A permanent home for British radiology

The Appeal Committee

Sir Jan Lewando, CBE (*Chairman*)
Professor G. H. du Boulay (*Appeal Co-Ordinator*)
Mr. L. F. Barr Smith
Dr. Julian Bloom
Sir Richard Doll, OBE, FRS
Mr. Kevin Hughes, OBE
Professor L. F. Lamerton
Sir Thomas Lodge
Dr. J. F. Loutit, CBE, FRS
Professor W. V. Mayneord, CBE, FRS
Professor J. H. Middlemiss, CMG
The Lord Penney, OM, KBE, FRS
Sir Edward E. Pochin, CBE
Sir John Read
Mr. C. F. E. Shakerley
Professor Sir David Smithers
Professor R. E. Steiner, CBE
Dr. Herman D. Suit
Dame Janet Vaughan, FRS
Professor Sir Brian Windeyer
The Lord Zuckerman, OM, KCB, FRS

The President of the Institute and Appeal Executive Committee members

Funds are still needed for the new permanent home for The British Institute of Radiology at 36 Portland Place, London W1, next door to the Royal College of Radiologists

Donations and ideas to:
Appeal Co-Ordinator, 32 Welbeck Street, London W1M 7PG (01–486 5084)

1981, *British Journal of Radiology*, 54, 179–186

VOLUME 54 NUMBER 639 MARCH 1981

The British Journal of Radiology

Radiation hazards: 25 years of collaborative research

Sylvanus Thompson Memorial Lecture, April 1980

By R. Doll, M.D., D.Sc., F.R.C.P., F.R.S.

Imperial Cancer Research Fund, Cancer Epidemiology and Clinical Trials Unit, 9 Keble Road, Oxford

(*Received July 1980*)

In studying the causes of disease, the research worker has three methods to choose from: laboratory experiment *in vitro* or on animals, clinical experiment on man, and observation of the circumstances in which disease in man occurs. Ethical considerations seriously limit the use of the second method for the study of potentially fatal conditions like cancer. In practice, the choice is commonly limited to the other two. The third, or epidemiological, method has many serious disadvantages. In particular, the circumstance in which man is exposed to a suspected aetiological agent cannot be altered to suit the requirements of the investigator and the results are difficult to interpret as the observed effects may be due to a variety of factors that are associated with one another, some of which the investigator can easily overlook. The method, however, also has some compensating advantages. One is that the results obtained relate directly to the animal whose disease we are trying to prevent, so that the uncertainty introduced by extrapolating from one species to another, without full comprehension of the effects of genetic differences, is avoided. In particular, they enable precise measures to be made of the size of an effect, something that can seldom be determined confidently by extrapolation. Another advantage is that people feed and house themselves and obtain medical care without cost to the investigator, so that much larger numbers can be studied than are usually possible in the laboratory and the size of even very small risks can be determined directly.

Epidemiological observations on large numbers, however, can seldom be made entirely by one person and recourse is commonly required to the records of many different doctors. In my experience the British medical profession has been particularly generous in providing the necessary information and my colleagues and I have obtained the assistance of many thousands of doctors in the course of our work over the past quarter of a century. Many of them have been members of The British Institute of Radiology, and I hoped that I might be able to go some way towards repaying our debt to them by reporting today some of the results of the research which they have made possible and which bear on the nature and extent of the hazards of ionizing radiation.

British Radiologists

One such study has been an examination of the mortality of British radiologists, which was begun by the late Professor Court Brown and myself in 1956, to test two hypotheses: we sought, firstly, to find out if repeated small doses of radiation received in the course of occupational exposure could result in a loss of life from such a wide variety of causes that they might be regarded as causing a non-specific increase in the rate of aging, and secondly to see if the same sort of dose could cause an increase in mortality from cancer other than cancer of the skin. In retrospect, it is fascinating to recall how strongly the second hypothesis, which is almost certainly true, was resisted; while the first, which is equally certainly not, was accepted. Within months of the report that small mammals had their lives shortened by a single sub-lethal dose of radiation or by chronic exposure at comparatively high dose rates, it was believed throughout the scientific world that whole-body doses of one roentgen would reduce the expectation of life by between one and five days (Hursch, 1956; Jones, 1957; Failla and McClement, 1957)—a remarkable illustration of what Trotter called "the mysterious viability of the false".

The results of the study of British radiologists were published in 1958 (Court Brown and Doll,

1958) and may, perhaps, have helped to restore a sense of proportion in that they showed that, whatever harm ionizing radiations might do, the total effect was so small that even doctors who had specialized in radiology from its earliest days suffered no higher mortality than either doctors in general or all men of the same socio-economic class.

In the subsequent 22 years, Michael Court Brown, Jack Boyd, and then Peter Smith and I have continued to record deaths among members of the original population and we can now report on the fate, almost up to today, of the male doctors and dentists who joined the original X-ray Society, the Roentgen Society, The British Institute of Radiology, the British Association of Radiologists, the Society of Radiotherapists of Great Britain and Ireland, and the Faculty of Radiologists (as it then was) between 1897, when the first of these societies was founded, and December 31, 1954. The results (which were reported in the lecture) are described in full in an accompanying article by Smith and Doll (1981a).

IRRADIATION *IN UTERO*

The second study to which I want to refer is the Oxford Childhood Cancer Survey that was begun by Dr. Stewart in 1954 and led to a series of reports between 1956 and 1975. I have not been involved with the study personally, apart from having had some of Dr. Stewart's colleagues attached to my department after she left Oxford; but I want to cite it because its important results could not have been obtained without the collaboration of literally hundreds of doctors.

The study was begun to seek an explanation for the progressive increase in the death rate from leukaemia in young children that had taken place in England and Wales between the two world wars. Ionizing radiations were under suspicion as a cause of leukaemia, and it seemed sensible to enquire whether children who developed the disease had been exposed to X rays as well as to a variety of other environmental factors to any greater extent than other children of the same age. As the disease in children was rare, the study was planned to cover the entire country, and arrangements were made for Dr. Stewart to receive copies of the death certificates of all children under ten years of age, later extended to 15 years of age, who died of malignant disease of all types, the original idea being that a comparison could be made between children who developed leukaemia and children who developed other types of cancer. Dr. Stewart could not herself cover the entire country, so she enlisted the help of Medical Officers of Health who were asked to interview the mothers of the dead children on her behalf, using a standard questionnaire. To provide a control group, the Medical Officers of Health were asked to select from the local birth registers surviving children of the same sex, who were born about the same time and were resident in the same region as that of the child with malignant disease with whom they were matched.

A preliminary report was published (Stewart *et al.*, 1956) which drew attention to the fact that a greater proportion of mothers of children who died of leukaemia or some other type of malignant disease, in comparison with mothers of children without malignant disease who were still surviving, reported that their abdomens had been X-rayed during the time the child was *in utero*, and the same observation has continued to be made on subsequent groups of children who died of malignant disease over the years 1953–67 (Stewart *et al.*, 1958; Hewitt *et al.*, 1966; Stewart and Kneale, 1968; Bithell and Stewart, 1975). Moreover, the excess history of irradiation given by the mothers of affected children was greater when the beam had been directed at the abdomen during the relevant period than when it had been directed to any other part of the body or at any other period in her history.

In a retrospective study of this sort, two hurdles have to be overcome before it is possible to conclude that the factor identified is likely to be a cause of the disease. Firstly it has to be shown that the memory of the person giving the history was not biased by knowledge of the occurrence of the disease; secondly, attention has to be given to the possibility that the association is secondary and due to an association of the factor in question with some other factor that is really the cause of the disease.

To be able to do this, Stewart and her colleagues were completely dependent on the collaboration of radiologists and other hospital staff throughout the country. First she had to show that the mother's statement that her abdomen had been X-rayed in pregnancy was correct. This presented no great difficulty as the radiologists' records provided objective evidence of a relevant X-ray in 91.9% of cases (92.7% for the mothers of children who developed cancer and 90.3% of the control mothers). Then she had to show that the mother's report that she had not been X-rayed was also correct. This was vital as, otherwise, it was always possible that a mother who had lost children from a mysterious disease would have been better at recalling the events of her pregnancy than other less motivated women. Eventually this was also done by checking the antenatal records of 2405 pairs of cases and controls. These showed that a positive record of an antenatal X-ray had not been reported by 0.6% of the mothers of the affected children and by 1.0% of the mothers of control children—a trivial difference that had no material effect on the results (Stewart *et al.*, 1958; Hewitt *et al.*, 1966).

The association was therefore not distorted by memory nor, from the design of the study, was it likely that a group of women had been selected as controls who had a special reason for avoiding radiological examination. There remained the possibility that the cause of the malignant disease, whatever it may have been, also caused the mother to be X-rayed. A hypothesis of this type can never be excluded entirely from observational studies, but three sets of data make it so unlikely that it is only reasonable to ignore it. First, intensive enquiry failed to elicit any other aspect of the obstetric history that could account for the facts. Secondly, the detailed information provided by the hospital radiologist showed that the excess risk increased in proportion to the number of X-ray exposures (Bithell and Stewart, 1975), and thirdly, as Mole (1974) showed, the excess mortality in irradiated twins was very similar to that in singleton births, despite the fact that a grossly higher proportion of twin pregnancies than of singleton pregnancies were X-rayed (Table I).

If these and other similar data are accepted as indicating that exposure to diagnostic X-ray procedures *in utero* caused an increased risk of malignant disease in the child (as I think they should be), it can be inferred that doses to the fetus of the order of 10 mGy (1 rad) cause a malignant tumour to develop in approximately one in every 2 000 children.

ANKYLOSING SPONDYLITIS

The third study that I have chosen to illustrate my theme is that of the long-term effects of radiotherapy given for the treatment of ankylosing spondylitis. This study was begun at the request of the Medical Research Council which had itself been requested to report to Parliament on the hazards to man of nuclear and allied radiations. The Committee that the Council set up did not take long to realize that there was very little information available that would enable it to assess the risk of small doses of radiation, and in July 1955 Michael Court Brown and I were asked to undertake the study as a matter of urgency, in the hope of obtaining some insight into the relationship between the dose of radiation and the subsequent incidence of leukaemia and aplastic anaemia. Moreover, we were asked to provide an answer for a committee meeting at 9.00 a.m. on the following January 1. With this remit it was easy to obtain collaboration and the study that was set up was planned to cover all patients treated for ankylosing spondylitis during the years 1935–54 at 82 radiotherapy centres throughout Great Britain, amounting to over 13 000 patients. Seventy-three radiotherapists and 45 other colleagues helped to extract and analyse the data, and at 1.30 a.m. on January 1, 1956, Court Brown and I obtained from a Hollerith card sorter a relationship between the mortality from leukaemia and the dose of radiation in terms of the whole-body integral dose.

TABLE I

RISK OF CHILDHOOD CANCER IN SINGLETONS AND TWINS BY ANTENATAL X-RAY EXPOSURE (AFTER MOLE, 1974).

	Singleton births	Twin births
Proportion X-rayed	10%	55%
Leukaemia by age 10 yrs		
incidence per 100 000		
X-rayed	34.6	26.3
not X-rayed	22.8	12.0
relative risk	1.5	2.0
Solid tumours by age 10 yrs		
incidence per 100 000		
X-rayed	39.3	30.9
not X-rayed	26.9	19.5
relative risk	1.5	1.6

The Committee was not satisfied with this finding, however, and asked to have the data re-analysed in terms of the dose to the spinal marrow. To obtain this a phantom had to be constructed and the doses that were received at three points in the spine from each of the many radiotherapy regimes used had to be measured. This was done by groups of physicists and engineers from the Institute of Cancer Research, the Middlesex and Mount Vernon Hospitals, the MRC Radiobiological Research Unit, and the National Institute of Medical Research. A fresh answer was obtained, and a preliminary assessment was presented to the Committee in May 1956 in time for the publication of a White Paper in June (Medical Research Council, 1956). A full report of the study was published the following year (Court Brown and Doll, 1957), when it was concluded that for low doses the incidence of leukaemia bore a simple proportional relationship to the dose of radiation and that a dose of one roentgen to the whole red marrow would produce each year between 1.0 and 1.6 cases of leukaemia per million irradiated subjects.

In the succeeding eight years the study was refined, a few centres and patients that had been omitted originally were added, and patients were followed up individually to January 1, 1960 (Court Brown and Doll, 1965; Doll, 1960). As a result it was possible to show that mortality from cancer was increased in practically every organ that was exposed to the beam (if not in every organ) and that the increase began about six years after treatment (or earlier in the case of leukaemia). Arrangements were then made to continue to follow the patients who had received no more than one course of treatment. Professor Ellis developed a computer programme that provided a much more accurate estimate of the mean marrow dose than had previously been available (Ellis *et al.*, 1975), and a new group of spondylitic patients who had never been irradiated were added to the study. In 1969, Michael Court Brown, who had been given the title of Professor in Edinburgh University while continuing to direct the Medical Research Council's Clinical Effects of Radiation Research Unit, died of a coronary thrombosis and the study has been continued in his memory by Peter Smith, one-time statistician in his Unit, and myself.

Smith and I are now able to report on the 14,111 patients who were first treated with X rays for ankylosing spondylitis between 1935 and 1954 and have been followed until their death, the end of the year following their second course of radiation treatment, the date they emigrated, or January 1, 1970, whichever was the earliest. We have limited the period of observation to that following the first period of treatment, with the exception referred to, as we were seeking to determine the duration of risk following exposure and this is made impossible by the intrusion of repeated treatments. We have, however, included the first year following a second course of treatment as newly induced cancers are most unlikely to appear within this period and because to have excluded it would have risked biasing the results, as the early symptoms of a cancer may sometimes be misdiagnosed as a recurrence of spondylitis and treated accordingly.

TABLE II

STATUS OF 14111 PATIENTS TREATED BY RADIOTHERAPY FOR ANKYLOSING SPONDYLITIS AT END OF FOLLOW-UP (1.1.70)

State at end of observation	No. of patients		Total (%)
	Male	Female	
Alive at 1.1.70, one course of treatment only	3649	771	4420 (31.3)
Alive at end of year following second course of treatment	6244	1211	7455 (52.8)
Dead	1498	261	1759 (12.5)
Emigrated	212	57	269 (1.9)
Untraced	173	35	208 (1.5)
All states	11776	2335	14111 (100.0)

TABLE III

MORTALITY FROM VARIOUS CAUSES AMONG 14111 SPONDYLITIC PATIENTS TREATED BY RADIOTHERAPY AND 1021 PATIENTS NOT SO TREATED COMPARED WITH MORTALITY EXPECTED FROM NATIONAL RATES

Cause of death	Irradiated patients		Unirradiated patients	
	No. of deaths observed	Ratio of numbers observed and expected	No. of deaths observed	Ratio of numbers observed and expected†
Leukaemia	31	4.79***	0	—‡
Cancer of "heavily irradiated sites"	259	1.55***	14	1.20
Cancer of "lightly irradiated sites"	79	1.20	4	0.72
Cancer of colon	28	1.62*	0	—‡
Other causes	1362	1.69***	113	1.83***
All causes	1759	1.66***	131	1.62***

*P < 0.05. ***p < 0.001.

†Excluding the first 18 months after entry to the study.

‡Expected deaths from leukaemia 0.44, from cancer of colon 1.42,.

Preliminary results were reported at a conference at the International Atomic Energy Agency in Vienna in 1978 (Smith and Doll, 1978) and a full account will be published shortly (Smith and Doll, 1981b).

The fate of the patients at the conclusion of the follow-up is shown in Table II. Those who received a second course of treatment were observed for an average of only 3.5 years; those who received only one course were observed for an average of 16.2 years.

Table III shows the numbers of deaths from five groups of causes and the ratios of the numbers observed to those expected from the national mortality rates for England and Wales. It also shows, for comparison, corresponding figures derived from following up 1021 spondylitic patients not treated by radiotherapy and reported by Smith *et al.* (1977). Deaths from cancer are divided into four categories: (i) leukaemia, (ii) other cancers arising in organs that were likely to have been directly in the treatment beams, (iii) other cancers arising in organs that would have received only a minimal dose of radiation through scatter from beams directed at other parts of the body, and (iv) cancer of the colon, which may be associated with spondylitis itself irrespective of irradiation because of the increased risk of ulcerative colitis in spondylitic patients.

Statistically significant excesses of death were observed for leukaemia, cancers of heavily irradiated sites, cancer of the colon, and all non-neoplastic causes in the irradiated series and for all non-neoplastic causes in the unirradiated series. Overall there was very little difference between the total mortality experience of the two series, but direct comparison is difficult because of the selective factors that must have influenced the choice of therapy (Radford *et al.*, 1978).

Table IV shows the number of deaths, the ratios of the numbers observed and expected, and the excess of mortality from leukaemia and other cancers of heavily irradiated sites at different times after treatment. Review of the case notes shows that the three patients who died of leukaemia within the first year (all of whom, in fact, died within three months) had developed their disease before entry to the study and that the disease might have prompted the treatment. These deaths and the corresponding period at risk should, therefore, be excluded from the analysis. Seven other cases of leukaemia, however, have been added which were not recorded as having been the underlying cause of death. In five instances leukaemia was recorded on the death certificate as a contributory cause and two others were diagnosed on review of the clinical records among the five patients whose death had been attributed to aplastic anaemia. To compensate for these additions the expected deaths were increased in the same proportion, *i.e.* by 25%*. The results show that the excess mortality from leukaemia had a peak three to eight years after irradiation and then fell, no excess mortality being observed in our series more than 20 years after irradiation.

Review of the case notes of patients with other types of cancer suggested that some patients who died of cancer within three years of treatment had had their disease before treatment was started, including several with tumours of the spinal nerves and pancreas and secondary tumours in the spine. The symptoms produced by these tumours almost certainly led to a misdiagnosis of recrudescent

TABLE IV

MORTALITY FROM LEUKAEMIA AND CANCER OF HEAVILY IRRADIATED SITES AMONG 14111 SPONDYLITIC PATIENTS BY TIME (YEARS) AFTER IRRADIATION

Cause of death	0–1	2	3–5	6–8	9–14	15–20	21 or more
Leukaemia:							
No. of deaths	3‡	4	12	7	6	6	0
Ratio of observed to expected	3.9	8.4	10.8	6.4	2.6	3.3	—
Excess death rate†	10.6	30.6	45.4	30.3	11.1	20.7	—
Cancers of heavily irradiated sites:							
No. of deaths	33		27	24	91	69	15
Ratio of observed to expected	1.66		1.39	1.16	1.80	1.58	1.14
Excess death rate†	40.4		31.4	16.3	122.4	125.3	39.2

†Per 100 000 persons per year.
‡All considered, on review of case notes, to have developed leukaemia before irradiation.

---

*After exclusion of the three patients who died of leukaemia within the first year of the study, there remained 28 who died of leukaemia. To these seven patients (*i.e.* 25%) were added who developed leukaemia but whose deaths were not attributed to it. It was therefore necessary to add 25% to the expected deaths after the first year of study.

UNIVERSITY COLLEGE OF MEDICINE LIBRARY C. U.

spondylitis and caused the treatment rather than the reverse. The first period of three years after the start of treatment should, therefore, be ignored. The remaining data suggest that the attributable risk was at a maximum nine to 20 years after irradiation and subsequently fell. The number of deaths observed more than 20 years after irradiation is however, still small. Only four more deaths would have had to occur in order to maintain the excess mortality at the same rate and a difference of this order is well within the bounds of random variation (comparison of excess 9–20 years and over 21 years, $P = 0.45$).

TABLE V

MORTALITY FROM CANCER OF DIFFERENT HEAVILY IRRADIATED SITES AMONG 14111 SPONDYLITICS

Site of cancer	No. of deaths	Ratio of observed to expected deaths
Pharynx	3	2.33
Oesophagus	10	2.04*
Stomach	39	1.34*
Pancreas	13	1.53
Larynx	3	1.33
Lung	111	1.41***
Ovaries	4	1.37
Bones (excluding nose and jaw)	3	3.13
Lymph glands (Hodgkins')	2	0.70
Other lymphoma	13	2.59***
Spinal cord and nerves	4	7.84***
Other and Uncertain sites	21	1.98***
All heavily irradiated	226	1.54***

*$P < 0.05$ ***$p < 0.001$

Table V shows the excess mortality from cancers of different sites limited to data from the third year after entry to the study. The excess was statistically significant for cancers of the oesophagus, stomach, lung, non-Hodgkin's lymphoma and myelomatosis combined, tumours of the spinal cord and nerves, and a residual group of other sites. There was, however, no significant heterogeneity between the ratios of observed to expected deaths, with the exception of that for tumours of the spinal cord, and these data suggest that most cancers are increased in incidence approximately in proportion to their normal incidence in the absence of irradiation.

Two other results of interest emerge from this study: the variation in the susceptibility to cancer induction with age and the relationship between the incidence of induced leukaemia and dose. Table VI shows the numbers of cases of leukaemia and the numbers of deaths from other cancers of heavily irradiated sites by the age of the patient at the time of irradiation. The table also shows the ratios of the numbers observed and expected and the estimated excess risks. Observations before the second year of the study are omitted in relation to leukaemia and before the third year of the study in relation to other cancers. It appears from Table VI that the ratio of observed to expected deaths remains approximately constant and the extra mortality from both leukaemia and solid tumours induced by irradiation increases with the age of the patient, at least from about 20 years of age. The youngest patient to be observed in this study was 14 years old at irradiation and no data have been obtained relating to younger ages.

If, as it appears, susceptibility to the induction of cancer by radiation increases with the age of the patient, this will inevitably modify the shape of the relationship obtained previously between the attributable mortality rate and the length of time following treatment. Mortality rates normally increase with age irrespective of irradiation, so that the proportion of elderly people under observation will of necessity decrease with the passage of time. Consequently the proportion of patients who are under observation more than ten years after irradiation will decrease progressively with age at irradiation. We must, therefore, recalculate the excess mortality rates, standardizing for the age of the subject at the time of treatment, when examining the trend with time after irradiation, and standardizing for time after irradiation when examining the trend with the age of the patient at the time of treatment. The results obtained in this way are given in the detailed report of Smith and Doll (1981b). They do not qualitatively alter the conclusions to be drawn from Tables IV and VI.

To obtain an estimate of the relationship between the dose of radiation and the subsequent incidence of leukaemia, we sought information in a standard form for a one in 15 sample of all patients, irrespective of outcome, and for all patients who died after a diagnosis of leukaemia had been made. As previously the period of observation in the year of first treatment and during the following year was excluded. We also excluded the three patients in our review with chronic lymphatic leukaemia, as the evidence suggests that the relationship, if any, between ionizing radiations and this condition is very different from that for the other principal clinical and cytological types. Examination of the excess mortality for the other forms of leukaemia in groups of patients receiving mean spinal marrow doses varying from less than 100 cGy (rad) to over 600 cGy (rad) suggests that the attributable mortality per cGy is

TABLE VI

MORTALITY FROM LEUKAEMIA AND CANCER OF HEAVILY IRRADIATED SITES AMONG 14111 SPONDYLITICS BY AGE AT IRRADIATION

Age at treatment (years)	Cases of leukaemia			Deaths from other cancers of heavily irradiated sites		
	No. observed	Ratio of observed to expected	Excess† incidence	Ratio of observed	Ratio of observed to expected	Excess mortality
14–25	1	2.00	3.0	5	1.89	15.7
25–34	8	4.74	15.0	29	1.49	25.2
35–44	9	4.21	20.7	80	1.71	111.3
45–54	10	5.76	53.9	69	1.43	151.0
55 & over	7	5.60	100.1	43	1.42	253.7
All ages	35	4.79	24.5	226	1.53	77.3

†Per 100000 persons per year

about 0.063 cases per 100000 men per year or about ten cases per 1000000 over a 15-year period, with an upper line of about 13 cases per 1000000 (Smith and Doll, 1981b). This estimate is slightly less than that obtained from observation of the survivors of the Hiroshima and Nagasaki explosions. The spondylitic population, however, would be expected to be less susceptible to the induction of leukaemia than the survivors of the atomic explosions, as it contained no children and a high proportion of young adults.

CONCLUSION

These investigations and others like them which have been carried out in Britain, Japan, and the U.S.A. (see UNSCEAR, 1977, for review) provide strong evidence that exposure to ionizing radiations in amounts that are insufficient to cause macroscopic tissue damage increases the risk of cancer in practically every organ, that the increase in risk is approximately proportional to the dose received down to doses of the order of 1 cGy (rad), that the increase varies with age, being greater in childhood and late middle age than in young adult life, that the risk of developing leukaemia attributable to irradiation is 10 to 20 per 1000000 persons per cGy (rad) whole-body exposure within 20 years, and that the same dose produces about three times as many deaths from solid tumours as cases of leukaemia. At the same time, these investigations have also shown that doses insufficient to produce macroscopic evidence of damage have no other detectable effect on life expectancy.

There are many reasons for using ionizing radiations in the modern world, so that quantitative conclusions of this kind are crucial to any rational system of control. In the present state of knowledge such conclusions can be reached only by direct observations on man. Since the risks are small, the number of observations required is large and valid results can be obtained only by the collaboration of many doctors who are willing to trust each other with confidential information about their individual patients.

Such collaboration has been traditional in medicine; but it has come to be questioned in recent years as a result of the growth of public concern about the way computers have made it easy for masses of information to be exchanged, brought together, collated, and analysed within a matter of seconds. In fields outside medicine, this valuable capacity has not always been used in the interests of the individuals concerned, and it is understandable that proposals should have been made to various Government committees that information relating to a named individual that had been obtained for one purpose should not be used for another without the individual's consent. Admirable as this is as a general principle, it would be seriously disruptive if applied unthinkingly in all circumstances. In particular, it would put an end to a whole range of epidemiological studies concerned with assessing the medical effects of changing social habits, conditions of life, industrial employment, and the use of drugs.

Seven years ago the Medical Research Council (1973), after consultation with the DHSS and the British Medical Association, issued a statement on responsibility in the use of medical information for research. "Medical information about identified individual patients should", it said, "continue to be made available without their explicit consent for the purposes of medical research", but subject to certain safeguards. The most important of these was that "all medical information that can be related to an identified individual should be treated as confidential and should be communicated only to medical research workers who are engaged in investigations in the interests of the health of the community and [then] only if, in the opinion of the medical practitioner holding that information, such communication will not harm the subject's interests". With that and the other safeguards listed by the Medical Research Council, exchange of information between doctors and medical research workers has continued and has led to a number of useful discoveries. It has not, to the best of my knowledge, ever been abused. I am personally extremely grateful to all the doctors who have helped in our research for their trust and for giving their time to seek out records and answer letters. I hope that some of it has been worthwhile and that our successors will be able to continue in the same fruitful way for many years to come.

REFERENCES

Bithell, J. F. and Stewart, A. M., 1975. Pre-natal irradiation and childhood malignancy: a review of British data from the Oxford survey. *British Journal of Cancer, 31*, 271–287.

Court Brown, W. M. and Doll, R., 1957. Leukaemia and aplastic anaemia in patients irradiated for ankylosing spondylitis. *Medical Research Council Special Report Series* No. 295. HMSO.

1958. Expectation of life and mortality from cancer among British radiologists. *British Medical Journal, ii*, 181–187.

1965. Mortality from cancer and other causes after radiotherapy for ankylosing spondylitis. *British Medical Journal, ii*, 1327–1332.

Doll, R., 1960. The carcinogenic risk of radiation: human leukaemia. *Acta Unionis Internationalis Contra Cancrum, 16*, 418.

Ellis, R. E., Healy, M. J. R., Schleien, B. and Tucker, T., 1975. A system for estimation of mean active bone marrow dose. *Bureau of Radiological Health*, DHEW Pub. (7DA), 76–8015.

Failla, G. and McClement, P., 1957. The shortening of life by chronic whole body irradiation. *American Journal of Roentgenology, 78*, 946–954.

Hewitt, D., Sanders, B. and Stewart, A., 1966. Oxford Survey of Childhood Cancers: progress report IV. Reliability of data reported by case and control mothers. *Monthly Bulletin of the Ministry of Health, 25*, 80–85.

Hursch, J. B., 1956. The effect of ionizing radiation on longevity. (University of Rochester, U.R. 506. Rochester, N.Y.).

Jones, H. B., 1957. The nature of radioactive fall-out and its effects on man. (U.S. Government Printing Office, Washington).

Medical Research Council, 1956. The hazards to man of nuclear and allied radiations. (HMSO, London, Cmd. 9780).

Medical Research Council, 1973. Responsibility in the use of medical information for research. *British Medical Journal, 1*, 213–216.

Mole, R. H., 1974. Antenatal irradiation and childhood cancer: causation or coincidence? *British Journal of Cancer, 30*, 199–208.

Radford, E. P., Doll, R. and Smith, P. G., 1977. Mortality among patients with analysing spondylitis not given X-ray therapy. *New England Medical Journal, 297*, 572–576.

Smith, P. G. and Doll, R., 1978. Age and time dependent changes in the rates of radiation induced cancers in patients with ankylosing spondylitis following a single course of X-ray treatment. In: *Late Biological Effects of Ionizing Radiations, vol. 1*, (International Atomic Energy Authority, Vienna), pp. 205–218.

1981a. Mortality from cancer and all causes among British radiologists, *British Journal of Radiology, 54*, 187–194.

1981b. Causes of death among patients with ankylosing spondylitis following a single treatment course with X-rays. In preparation.

Smith, P. G., Doll, R. and Radford, E. P., 1977. Cancer mortality among patients with ankylosing spondylitis not given X-ray therapy. *British Journal of Radiology, 50*, 728–734.

Stewart, A. M. and Kneale, G. M., 1968. Changes in cancer risk associated with obstetric radiography. *Lancet, i*, 104–107.

Stewart, A. M., Webb, J., Giles, D. and Hewitt, D., 1956. Malignant disease in childhood and diagnostic radiation in utero. *Lancet, ii*, 447.

Stewart, A. M., Webb, J. and Hewitt, D., 1958. A survey of childhood malignancies. *British Medical Journal, i*, 1495–1508.

UNSCEAR, 1977. Sources and effects of ionizing radiation. United Nations Scientific Committee on the effects of Atomic Radiation. (United Nations, New York).

1981, *British Journal of Radiology*, *54*, 187–194 MARCH 1981

Mortality from cancer and all causes among British radiologists*

By †P. G. Smith, B.Sc. and R. Doll, M.D., D.Sc., F.R.C.P., F.R.S.

Imperial Cancer Research Fund, Cancer Epidemiology and Clinical Trials Unit, 9 Keble Road, Oxford

(Received July 1980)

ABSTRACT

The mortality of men who joined a British radiological society between 1897 and 1954 has been compared with that of (i) all men in England and Wales, (ii) men in social class 1, and (iii) male medical practitioners. Radiologists who entered the profession before 1921 suffered a death rate from cancer 75% higher than that of medical practitioners. Among these men there was a statistically significant excess of deaths from cancers of the pancreas (6 against 1.9 expected), lung (8 against 3.7), and skin (6 against 0.8), and from leukaemia (4 against 0.7).

There were 72 deaths from cancer among men who entered the study after 1920 and 68.6 deaths were expected, based upon rates among medical practitioners. For no individual cancer site did the observed number of deaths exceed the expected number. There was some evidence, however, that the ratio of observed to expected cancer increased with the duration of time that men were included in the study. Among those followed for more than 30 years there were 30 deaths against 22.1 expected. It is not possible to make a close estimate of the dose of radiation received by the men in this study, but those who entered between 1920 and 1945 could have received an accumulated whole-body dose of the order of 1–5 Gy (100 to 500 rad).

For all non-cancer causes of death combined, the death rate among radiologists is lower than that among all men in England and Wales, men in social class 1, and male medical practitioners. The data offer no support for the concept of a non-specific aging effect of radiation.

There is overwhelming evidence that persons exposed to large doses of radiation suffer an increased risk of death from leukaemia and from other cancers (for a recent review see UNSCEAR (1977)), but a number of major issues concerning the medical effects of ionizing radiations have yet to be resolved. One is the magnitude of the carcinogenic risk associated with chronic exposure to low doses of radiation. It has, for example, been postulated that the effects of such radiation may be considerably greater than has been estimated by linear extrapolation from the effects observed in populations exposed to high radiation doses at high dose rates. Another is whether radiation exposure produces non-specific aging and reduces longevity by increasing death rates from all causes rather than by affecting death rates from cancer only. The mortality experience of radiologists is relevant to both of these issues. We have, therefore, sought to extend the study of Court Brown and Doll (1958) who reported on the mortality of British radiologists, from all causes and from cancers of specific sites, up to 1957.

THE STUDY POPULATION AND METHODS

A detailed description of the study population was given by Court Brown and Doll (1958) and we give here only a brief summary. The records of The British Institute of Radiology and the Royal College of Radiologists (and of their antecedent societies) were searched to identify those members who had medical or dental qualifications and who had joined either of the societies between 1897 and 1954. The small number of women members was excluded from the study group but those who were abroad in the Colonial or Armed Services at the time of first registration with the societies were included. The number of men in this latter group is, however, also small and we have preferred to exclude them from the present analysis (apart from those who resided in Eire), because of the difficulty of tracing them.

A variety of methods have been used to determine the status of the remaining 1338 members of the study group on January 1, 1977. The records of the radiological societies enabled us to trace many of the men; where these were inadequate, we endeavoured to obtain the required information through approaches to the General Medical Council, the British Medical Association, other professional organizations, the National Health Service Central Register, the hospitals in which the members worked, or in some instances the members themselves or their relatives. When an individual could not be traced by these means, we searched the quarterly alphabetic indices of all deaths in England and Wales, compiled by the Registrar General, for a period of a year or so after contact was lost. In these ways it has been possible to determine either that an individual was alive on January 1, 1977, or that he had died or emigrated before that date, for all but five of the 1338 men in the study population. The five men who could not be traced have been included in the analysis until the time at which they could no longer be traced, which was, on average, 31 years after they first entered the study.

---

*Part of this material was presented by Sir Richard Doll in the Sylvanus Thompson Memorial Lecture, April 1980.

†Present address: Department of Epidemiology and Medical Statistics, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT.

Death certificates were obtained for radiologists who had died and, for those who had died of cancer, the cause of death was coded according to the 7th Revision of the International Classification of Diseases and Causes of Death (World Health Organisation, 1957). In a few instances death certificates could not be located but, with two exceptions, we were able to determine the cause of death from hospital records. For two men we know only that they died in 1917 and 1967 respectively.

For most of the analyses we shall present, men who emigrated to countries other than Eire have been excluded from the study from the date they left the country. We have, however, followed and successfully traced all the men who had joined one or other radiological society before 1921. We did this because the British X-ray and Radium Protection Committee was formed in 1921 and issued its first recommendations in July of that year. Those who joined before 1921 are, therefore, of particular interest as they were working during a period when protective measures against radiation exposure were frequently not employed. Twenty of them had emigrated. All were found to have died and in each case we were able to ascertain the cause of death. It has, therefore, proved possible to follow this particular group of subjects through to extinction.

Calculation of expected deaths

The numbers of deaths expected were estimated by multiplying the number of man-years at risk during the period of the study by corresponding mortality rates derived from national statistics for England and Wales. The numbers of years at risk were calculated separately for each five-year age group up to the age of 85 years and for 85 years and over, for the period 1897–1915, for each quinquennial period from 1916–1920 to 1966–1970, and for the period 1971–1976.

Three sets of mortality rates were used for comparison with the death rates among radiologists. These were based on published data for England and Wales and related to deaths among (i) all men, (ii) men in social class 1 and (iii) male medical practitioners. Death rates for all men from all causes, all neoplasms and cancers of specific sites were taken from Case *et al.* (1976). The rates are published separately for men in each of the five-year age groups 0–4 years up to 80–84 years and for 85 years or more for each of the quinquennial periods from 1911–1915 to 1966–1970. (Rates for the period 1971–1975 were kindly supplied by Professor M. R. Alderson). Rates for 1911–1915 were used for the period 1897–1915 and those for 1971–1975 were used for 1971–1976. Death rates for men in social class 1 and for male medical practitioners are not published annually by the Registrar General but his occupational mortality reports give standardized mortality ratios (SMR)* for men in social class 1 and for medical practitioners for the years 1910–1912, 1921–1923, 1930–1932, 1949–1953, 1959–1963 and 1970–1972. For all causes and for all cancers combined, SMRs are given for men in different age groups (usually these age groups include 20–24 years, 25–34, 35–44, 45–54 and 55–64 years). Calculated SMRs for men aged over 64 years are unreliable as the previous occupation of men who have retired is often poorly recorded in the national censuses and we have assumed that the SMRs for men aged 55 to 64 years provide a better estimate of the SMRs for men aged 65 years or more than those which are published. To estimate the mortality rates for men in a particular age group and quinquennial period we have interpolated the data given in the occupational mortality reports. For example, the death rate from all neoplasms for men in England and Wales aged 45–49 years in 1936–1940 was 1292/million/year. In 1930–1932 the SMR for all neoplasms for men in social class 1 aged 45–54 years was 88 and in 1949–1953 the corresponding SMR was 82. To estimate the mortality rate for men in social class 1 in 1936–1940 we multiplied the death rate for all men by an average of these two SMRs weighted according to the time between the occupational mortality reports and 1936–1940. Thus we estimated the mortality rate for men in social class 1 to be

$$1292\,(7\times 0.82+13\times 0.88)/(7+13)=1110/\text{million}/\text{year}.$$

We assumed that the SMRs for men in a ten-year age grouping applied to each of the two five-year groupings. SMRs for 1910–1912 were used for all rates prior to 1911 and SMRs for 1970–1972 were used for the rates for 1971–1976.

A similar procedure was used to estimate death rates from cancers of specific sites for men in social class 1, but we have assumed that the SMR was the same in all age groups as figures are not published separately for different age groups. SMRs for specific cancers have been published for medical practitioners only in recent occupational mortality reports and only some of the sites in which we were interested are included. We have not, therefore, been able to estimate site-specific rates for this group.

---

*An SMR is the ratio of the death rate in the group of interest (*e.g.* those in social class 1) to the death rate in all men, multiplied by 100. Thus, for example, an SMR of 88 implies that the death rate is 88% of the rate for all men.

Cancer death rates for England and Wales are available as far back as 1911 due to the work of Case *et al.* (1976). Unfortunately rates for causes other than cancer have not been similarly complied for so long a period. The compilation of such rates presents formidable difficulties, because of the extensive changes in disease classification which have taken place. We have not, therefore, been able to compare the mortality rates of radiologists from specific causes other than cancer with national mortality rates; the only such comparison we have made is for all non-neoplastic causes combined.

TABLE I

STATE OF THE STUDY GROUP OF 1338* RADIOLOGISTS AT 1.1.1977

State at 1.1.77	Number who entered study:		Total (%)
	Prior to 1921	After 1920	
Dead	319	411	730 (54.6)
Alive	0	494	494 (36.9)
Emigrated	20	89	109 (8.1)
Lost	0	5	5 (0.4)
Total	339	999	1338 (100.0)

*1381 men were included in the original report of Court Brown and Doll (1958). Our analysis includes fewer men as we have excluded all radiologists who were not resident in the United Kingdom or Ireland when they first registered with one of the radiological societies.

RESULTS

Of the 1338 radiologists included in the study 730 (54.6%) had died by January 1, 1977, 109 (8.1%) had emigrated and 494 (36.9%) were still alive and resident in Great Britain or Eire. We were unable to trace five (0.4%). Of the 339 radiologists who entered the study prior to 1921 all had died, including the 20 who had emigrated (Table I).

The numbers of deaths among radiologists from all causes and all neoplasms are compared in Table II with the expected numbers based on rates for all men in England and Wales, for those in social class 1, and for male medical practitioners. In general, death rates among men in social class 1 and among male medical practitioners are lower than rates among "all men". This is reflected in Table II in which the expected numbers for deaths based upon death rates for all men are higher than the numbers based on the rates for the other two groups in all but one cell of the Table. Radiologists are classified in social class 1 and it therefore seems appropriate to compare their mortality with that of men in this social group. Comparison with medical practitioners would, perhaps, be better but unfortunately we have been unable to estimate death rates for cancers of specific sites for this group. Comparisons of mortality from broad groups of causes are, therefore, made with male medical practitioners and from individual types of cancer with men in social class 1.

Mortality among those who entered prior to 1921

For radiologists who entered the study prior to 1921 the number of deaths from all causes is not

TABLE II

OBSERVED AND EXPECTED NUMBERS OF DEATHS FROM CANCERS AND ALL OTHER CAUSES AMONG RADIOLOGISTS WHO ENTERED THE STUDY PRIOR TO 1921 OR AFTER 1920

Cause of death	Observed (O) and expected (E) numbers of deaths								
	Entry prior to 1921			Entry after 1920			All radiologists		
	O	E	O/E	O	E	O/E	O	E	O/E
All causes	319	(1) 334.42	0.95	411	541.77	0.76***	730	876.20	0.83***
		(2) 308.03	1.04		461.14	0.89*		769.18	0.95
		(3) 327.97	0.97		469.97	0.87**		797.94	0.91**
All neoplasms	62	(1) 49.11	1.26*	72	114.93	0.63***	134	164.04	0.82**
		(2) 43.07	1.44**		91.07	0.79*		134.13	1.00
		(3) 35.39	1.75***		68.65	1.05		104.04	1.29**
Other causes	257†	(1) 285.31	0.90*	339†	426.84	0.79***	596	712.16	0.84***
		(2) 264.96	0.97		370.07	0.92		635.05	0.94
		(3) 292.58	0.88*		401.32	0.84**		693.90	0.86**

(1) Based on rates for all men in England and Wales.
(2) Based on rates for social class 1.
(3) Based on rates for medical practitioners.
† includes one death with unknown cause.

*P < 0.05 }
**P < 0.01 } One sided in direction of difference.
***P < 0.001 }

significantly different from the expected number, regardless of the comparison group from which the latter is derived. The early entrants do, however, show an excess of deaths from cancer, which is most marked when comparison is made with the expected number based on rates for medical practitioners (62 deaths observed against 35.4 expected; $P<0.001$). In contrast, there is a deficit of deaths from causes other than cancer, which is about 10% of the expected number and statistically significant ($P<0.05$) when comparison is made with national death rates and with the rates among doctors.

All of the 339 radiologists who entered the study prior to 1921 are known to have died and, in Table III, we have compared the numbers of deaths from all causes and from cancers of specific sites with the numbers expected based upon mortality rates among those in social class 1 together with expected numbers for all causes, all neoplasms, and all other causes, based on mortality rates among medical practitioners. In these comparisons we have included the experience of the radiologists after they had emigrated. The number of deaths from all causes (339) is similar to the number expected among men in social class 1 (324.2) or among medical practitioners (344.8*). A statistically significant excess of deaths from all neoplasms was found in the earlier study of Court Brown and Doll (1958) and such an excess is still present in the up-dated results. The significant excess of deaths from cancers of the skin and pancreas was also reported by Court Brown and Doll (1958), but they did not find the significant excess of deaths from lung cancer and leukaemia which is now apparent. The ratios of observed to expected deaths which they reported for these neoplasms were, in fact, similar to those shown in Table III, but they were based on smaller numbers. The number of deaths from cancer of the rectum and from a residual group of other neoplasms are less than the expected numbers, but not significantly so. For each of the remaining five sites shown in the table there is a slight excess of the observed number of deaths over the expected number.

TABLE III

Number of observed and expected† deaths among the 339 radiologists who entered the study before 1921 (including emigrants)

Cause of death	Observed	Expected	O/E
All causes	339	324.24 (344.79)	1.05 (0.98)
All neoplasms	64	45.39 (37.18)	1.41 ** (1.72)***
Ca. oesophagus	3	2.55	1.18
Ca. stomach	7§	5.81	1.20
Ca. intestines	9	7.03	1.28
Ca. rectum	2	4.58	0.44
Ca. pancreas	6	1.86	3.23 *
Ca. lung	8	3.67	2.18 *
Ca. prostate	7	4.36	1.61
Ca. bladder	3	1.78	1.69
Ca. skin	6	0.77	7.79 ***
Leukaemia	4	0.65	6.15 **
Other neoplasms	9‡	12.33	0.73
All other causes	275‖	278.85 (307.61)	0.99 (0.89)†

*Asterisks indicate degree of significance as in Table II.

†Based on death rates for social class 1, except for numbers in parentheses which are based on death rates for medical practitioners.

‡These neoplasms were: Lip, Tongue, Gall Bladder and Liver, Abdominal, Testis, Glioma, Osteosarcoma, Bone Marrow, Lipoma, Small Intestine.

‖Includes one for whom the cause of death is not known.

§In the previous report (Court Brown and Doll, 1958) there were eight deaths from cancer of the stomach. One of these men was abroad when he first entered a radiological society and thus is among those who were excluded from the present study.

Tables IV and V show the number of deaths from all cancers and from all causes that occurred at different times after first registration as a member of one of the societies, in comparison with the numbers expected from the experience of male medical practitioners. For men who first registered before 1921 the trend in the ratio of observed to expected deaths is not significant for either group of causes. It is notable, however, that the ratio for all neoplasms is substantially higher twenty or more years after registration than in the earlier period (1.98:1 against 1.25:1).

Mortality among those who entered after 1920

Radiologists who entered the study after 1920 show a significant deficit of deaths from all causes combined and fewer deaths from causes other than cancer, but, in the latter case, the deficit is statistically significant only when comparison is made with the rates for all men and for all doctors (Table II). Deaths from cancer, in contrast, were significantly lower than those expected from the experience of

---

*The expected number of deaths based upon rates among medical practitioners exceeds the total number of radiologists in the study (339). The explanation for this apparent anomaly relates to a special use by epidemiologists of the term "expected number of deaths". This term is used to describe the number of deaths that would be required if the ratio of the number of observed deaths to the number expected corresponds to the ratio of the average annual death rate for those in the study group to that for members of the comparison population. Thus if we observe, as shown in Table III, 339 deaths and the "expected" number is 344.8, this should be interpreted as indicating that the average annual mortality rate in the study group is 0.98 times (339/344.8) the rate among all medical practitioners.

Mortality from cancer and all causes among British radiologists

TABLE IV

NUMBER OF OBSERVED (O) AND EXPECTED† (E) DEATHS FROM ALL NEOPLASMS BY TIME SINCE ENTRY INTO THE STUDY

Time since entry (years)	Year of first registration						Total		
	< 1921			1921+					
	O	E	O/E	O	E	O/E	O	E	O/E
0–	6	4.04	1.49	5	7.72	0.65	11	11.76	0.94
10–	8	7.14	1.12	13	15.82	0.82	21	22.96	0.91
20–	18	9.53	1.89	24	23.01	1.04	42	32.54	1.29
30–	18	8.33	2.16	23	15.55	1.48	41	23.88	1.72
40+	12	6.35	1.89	7	6.55	1.07	19	12.90	1.47
Total	62	35.39	1.75	72	68.65	1.05	134	104.04	1.29
χ_1^2 (trend)		1.42			3.02 ($P< 0.05$)‡			5.43 ($P< 0.01$)‡	

†Based on death rates for medical practitioners.
‡One-sided test.

TABLE V

NUMBER OF OBSERVED (O) AND EXPECTED† (E) DEATHS FROM CAUSES OTHER THAN NEOPLASMS BY TIME SINCE ENTRY INTO THE STUDY

Time since entry (years)	Year of first registration						Total		
	< 1921			1921+					
	O	E	O/E	O	E	O/E	O	E	O/E
0–	22	34.80	0.63	46	52.02	0.88	68	86.82	0.78
10–	46	53.12	0.87	82	85.88	0.95	128	139.00	0.92
20–	61	68.08	0.90	80	118.88	0.67	141	186.96	0.75
30–	63	70.68	0.89	84	96.35	0.87	147	167.04	0.88
40+	65	65.90	0.99	47	48.20	0.98	112	114.10	0.98
Total	257	292.58	0.88	339	401.32	0.84	596	693.90	0.86
χ_1^2 (trend)		2.45			0.01			1.38	

†Based on death rates for medical practitioners.

TABLE VI

NUMBER OF OBSERVED (O) AND EXPECTED† (E) DEATHS AMONG 999 RADIOLOGISTS WHO ENTERED THE STUDY AFTER 1920

Cause of death	Year of first registration						Total (1921–1954)		
	1921–1935			1936–1954					
	O	E	O/E	O	E	O/E	O	E	O/E
Ca. oesophagus	0	1.93	—	0	1.12	—	0	3.06	0.00*
Ca. stomach	4	5.44	0.74	2	3.40	0.59	6	8.84	0.68
Ca. intestines	4	6.23	0.64	2	3.66	0.55	6	9.89	0.61
Ca. rectum	2	3.72	0.54	0	2.05	—	2	5.77	0.35
Ca. pancreas	4	2.73	1.47	0	2.28	—	4	5.02	0.80
Ca. lung	13	11.58	1.12	10	12.24	0.82	23	23.82	0.97
Ca. prostate	2	5.06	0.40	3	2.00	1.50	5	7.06	0.71
Ca. bladder	1	2.34	0.43	1	1.54	0.65	2	3.88	0.52
Ca. skin	2	0.57	3.51	0	0.44	—	2	1.02	1.96
Leukaemia	3	1.29	2.33	1	1.30	0.77	4	2.59	1.54
Other neoplasms	13	10.70	1.21	5	9.44	0.53	18	20.12	0.89
All neoplasms	48	51.59 (38.50‡	0.93 1.25)	24	39.47 (30.15	0.61** 0.80)	72	91.07 (68.65	0.79* 1.05)

*Asterisks indicate degree of significance as in Table III.
†Based on death rates for social class 1.
‡Numbers in parentheses are based upon death rates for medical practitioners.

"all men" or men in social class 1, but slightly higher than that expected in comparison with doctors (72 deaths observed against 68.6 expected; $P< 0.10$).

Deaths from cancers of specific types are shown in Table VI, in comparison with those expected for the experience of men in social class 1. Data are shown separately for men who first registered before and after the end of 1935, as men in the latter group are likely to have been exposed to smaller amounts of radiation than those registering earlier. Overall there is a significant deficit of deaths from all neoplasms combined (72 deaths against 91.07 expected from social class 1 rates; $P<0.05$) but it should be noted that this deficit disappears if the expected number is based upon death rates among doctors (Table II). For none of the individual sites shown in Table VI is the number of deaths significantly greater than expected, but there is a significant deficit of deaths from cancer of the oesophagus (none observed, 3.1 expected; $P=0.047$ (one-sided)). The only two cancers for which there is an overall excess are cancer of the skin and leukaemia. Five of the six deaths from these causes were in radiologists who registered before 1936. Two of the four deaths from leukaemia were certified as being due to chronic lymphatic leukaemia (Table VII) whereas 0.7 were expected. Among those registered prior to 1921 there was one death from this cause (about 0.2 expected) so that overall, in both groups combined, there was a total of 3 such deaths against 0.87 expected ($P=0.06$, one-sided).

It should be noted, however, that although the overall mortality from cancer was so similar to that in doctors there was a suggestion of a progressive increase in mortality with time since first registration (Table IV) which is just statistically significant using a one-sided test ($P<0.05$). For the first twenty years after registration the ratio of observed to expected deaths was 0.76 to 1, whereas subsequently it was 1.20 to1. Moreover no such trend was apparent for deaths from all other causes (Table V).

Discussion

Deaths from cancer

In the previous follow-up of this population to 1957 a significant excess of deaths from cancer was found among men who entered the practice of radiology before 1921 (Court Brown and Doll, 1958). Further follow-up of this group of pioneer radiologists shows that up to 1977 their cancer mortality was 75% higher than that of other medical practitioners and that more than 20 years after first joining the mortality has become nearly 100% higher (48 deaths against 24.2 expected). This increase with time is not surprising as: (i) men who were already sick would be unlikely to enter one of the societies, (ii) the induction period for radiation-induced cancer, other than leukaemia, is usually more than 10 years, and (iii) the accumulated dose of radiation increases with length of membership.

Examination of mortality from cancers of specific sites had to be restricted to comparison with that of men in social class 1, and it should be borne in mind when interpreting our results that the death rate from all cancers combined was about 20% higher among men in social class 1 than among medical practitioners during the period that the pre-1921 radiologists were followed up. Since the last report no further deaths from skin cancer or from pancreatic cancer occurred in those who entered before 1921 but there were three more deaths from lung cancer and two from leukaemia and the excess of deaths from each of these four causes is now statistically significant. It should also be noted that two radiologists who entered the population before 1921 died of aplastic anaemia. These deaths were discussed in the previous report, when it was

TABLE VII

Deaths from leukaemia among radiologists

Ref. no.	Year of entry	Age at entry (years)	Interval from entry to death (years)	Leukaemia type
1439	1914	36	30	Monocytic
1873	1917	45	9	Acute lymphatic
1450	1918	30	57	Not specified
2345	1920	33	52	Chronic lymphatic
1780	1924	44	38	Myeloid
1589	1930	40	41	Acute
1866	1931	41	21	Chronic lymphatic
1495	1941	44	21	Acute following chronic lymphatic

suggested that one or both might have been due to acute aleukaemic leukaemia. No statistically significant excess of deaths from cancer of any other individual site occurred and the total number of cancer deaths other than those due to the four specific sites is 40 compared with an expected number based on social class 1 rates of 38.4.

It must be borne in mind, however, that the site-specific comparisons had to be made with men in social class 1 rather than with male medical practitioners which we believe would have been more appropriate. If the lower mortality of doctors compared with all men in social class 1 affected all sites equally the radiologists would have shown a statistically significant excess of all cancers other than leukaemia and skin cancer of 50% over that in doctors (54 deaths against 36.02 expected*) and, in the light of all other experience (UNSCEAR, 1977), it is, we believe, more appropriate to conclude that they experienced an increased mortality from cancer in general and a specific excess from skin cancer and leukaemia than that they experienced an excess mortality from cancer of four sites alone.

Men who first joined one or other of the radiological societies after 1920 had a lower overall mortality rate from cancer than men in social class 1 but about the same mortality as medical practitioners (72 deaths against 68.6 expected). Compared with doctors, there was a 25% excess of cancer deaths among men who entered radiological practice in the period 1921–1935. This is not statistically significant but it seems likely that some of these cancers may have been radiation induced. One of the two skin cancer deaths was due to cancer of the anus; the other due to a cancer of the skin of the hand and is most likely to have been caused by radiation exposure. The victim had been in radiological practice before 1921, though he did not join one of the societies until 1922 and is likely to have had considerable exposure in the earlier period (Mayneord, personal communication). Some of the others who died of cancer may also have been exposed to radiation prior to 1921.

The data provide some evidence that an excess of deaths from cancer in men who first joined one or other society after 1920 may be emerging at long periods after first exposure. The trend in the ratio of observed to expected deaths (Table IV) is only just statistically significant; but it does indicate that it would be worthwhile to continue to monitor the mortality experience of these men in the future and particularly to separate men who entered before 1936 (in whom there is more suggestion of a risk) from those who entered later.

It is of interest that among all the radiologists there were three deaths from chronic lymphatic leukaemia against about 0.9 expected. This form of leukaemia has not been found to be in excess in other studies of populations exposed to radiation. The radiologists have been followed for longer than most other populations, but this is unlikely to be the explanation of the difference as two of the three deaths from chronic lymphatic leukaemia occurred 21 years after the men had entered a radiological society and many other populations exposed to radiation have been followed at least as long as this. The excess is not quite statistically significant and it may be a chance finding.

Several studies have shown an excess of deaths from myeloma among those exposed to radiation (see Cusick (1980) for review). There were no deaths from this cause among the radiologists during the study period compared with about one expected. One radiologist who entered the study in 1919 is known to have died of myeloma less than a year after its close and another who entered in 1899 is known to have had myeloma in 1972, when he committed suicide.

Unfortunately there is very little information available on the extent of the radiation exposure of men included in our study. Among those who were in practice before 1921 the accumulated dose of radiation is likely to have been large. Court Brown and Doll (1958) have summarized how protective measures were introduced progressively in the early decades of this century; but such measures were not used in the earliest periods.

The experience of those who entered radiology after 1920 is more relevant to an assessment of the carcinogenic effects of frequent exposure to low doses. Our data are compatible with the view that the protective measures that came into widespread use in and after 1921 may have eliminated the risk of developing a radiation-induced cancer. We cannot, however, exclude the possibility that such a risk remains, as the total observed and expected numbers of deaths from cancer among those who entered after 1920 are not large (observed: 72, expected: 68.6, ratio: 1.05) and the confidence limits on the observed to expected ratio are quite wide (90% confidence interval: 0.85, 1.28). Moreover, the excess mortality was greatest 30 or more years after first entering the study (30 deaths against 22.1 expected) when the accumulated dose would have

---

**i.e.* 43.97 × 37.18/45.39. If cancers of the lung and pancreas are also similarly excluded there would be 40 deaths from other cancers against 31.49, a non-significant excess of 27%.

been greatest and a sufficient time for the induction of cancer would have passed.

It is not possible to make a close estimate of the dose of radiation likely to have been received by this group of radiologists. Current records suggest that present exposures are likely to be about 1 mGy (0.1 rad) per year or less. It was, however, substantially higher in the past and may have been as much as 50 mGy (5 rad) per year in the early fifties and perhaps double that earlier. It may therefore be assumed that the individual radiologists who first joined one or other of the societies before 1945 (which would have given them an opportunity of being observed more than thirty years after entry) could have received whole body doses of the order of 1–5 Gy (100 to 500 rad).

Deaths from causes other than cancer

In most studies of populations that have been exposed to radiation little evidence has been found that such exposure produces a non-specific aging effect. Increased mortality rates have been confined to cancers and rates of other causes of death have appeared to be unaffected (Beebe *et al.*, 1978). The notable exception is the study of American radiologists. The mortality experience of that group was compared with that of other medical specialists among whom exposure to radiation is likely to have been considerably lower (Matanoski *et al.*, 1975a, b). Those who joined the Radiological Society of North America in 1920–1929 or in 1930–1939 were found to have higher death rates from causes other than cancer than those who joined societies for otolaryngologists or ophthalmologists and slightly higher rates than men who joined the American College of Physicians. Non-cancer death rates in those who joined any of the societies in 1940–1949 were found to be similar.

In our study we can find no evidence to support the concept of a non-specific aging effect of radiation. Data were not available to us to examine whether the mortality of radiologists was different from that of other men for individual causes (other than cancer), but for all non-cancer causes of death combined there is no excess of deaths among radiologists. In fact they seem to have experienced lower death rates than other medical practitioners (Table II). Also there is no evidence of any excess emerging with longer periods of follow-up. Among those radiologists who were observed 40 years or more after joining one of the societies there have been 112 deaths from causes other than cancer whereas 114.1 would be expected based on rates among medical practitioners.

The data reported here include most of the observations reported on radiologists by Doll and Peto (1977) in their examination of the mortality of different groups of medical specialists. That study, which covered a much shorter period, included only 39 radiologists who were not also included in the present study and the two sets of results should not be added together.

Acknowledgments

We would like to thank the Council of the Royal College of Radiologists and The British Institute of Radiology for their co-operation in helping us trace the individuals in this study. The National Radiological Protection Board was kind enough to obtain some information on the doses of radiation to which radiologists had been exposed and Dr. Eric Smith also advised us on this issue.

We are grateful to Professor L. Lamerton and to a number of radiologists who helped and advised us on various aspects of the study.

We much appreciate the help of Barbara Hafner and Mary Burgess in tracing the individuals in the study and that of Carol Hermon in the statistical analysis.

REFERENCES

Beebe, G. W., Land, C. E. and Kato, H., 1978. The hypothesis of radiation-accelerated aging and the mortality of Japanese A-bomb victims. In: *Late Biological Effects of Ionizing Radiation*, Vol. 1. (International Atomic Energy Agency, Vienna).

Case, R. A. M., Coghill, C., Davies, J. M., Marley, J. L., Hytten, C. A., Pearson, J. T., Williard, S. R. and Alderson, M. R., 1976. Serial Mortality Tables. Neoplastic Diseases Volume 1. England and Wales 1911–70. (Division of Epidemiology. Institute of Cancer Research, London).

Cusick, J., 1981. Radiation-induced myelomatosis. *New England Journal of Medicine, 304*, 204–210.

Court Brown, W. M. and Doll, R., 1958. Expectation of life and mortality from cancer among British radiologists. *British Medical Journal, ii*, 181–187.

Doll, R. and Peto, R., 1977. Mortality among doctors in different occupations. *British Medical Journal, i*, 1433–1436.

Matanoski, G. M., Seltser, R., Sartwell, P. E., Diamond, E. L. and Elliott, E. A., 1975a. The current mortality rates of radiologists and other physician specialists: death from all causes and from cancer. *American Journal of Epidemiology, 101*, 188–198.

1975b. The current mortality rates of radiologists and other physician specialists: specific causes of death. *American Journal of Epidemiology, 101*, 199–210.

United Nations Scientific Committee on the Effects of Atomic Radiation, 1977. Sources and Effects of Ionizing Radiation (United Nations, New York).

World Health Organization. Manual of the international statistical classification of disease, injuries and causes of death. 7th ed., 1957. (World Health Organization, Geneva).

1981, *British Journal of Radiology*, *54*, 195–202 MARCH 1981

Clinical relevance of radiological abnormalities of the craniovertebral junction*

By E. H. Burrows, M.Rad., F.R.C.R.

Wessex Neurological Centre, Southampton General Hospital, Southampton SO9 4XY

(Received September 1980)

ABSTRACT

Clinical review of a large series of lesions of the craniovertebral angle revealed that no abnormality could be shown by radiological means in 30–50% of cases. Conversely, 30–50% of radiologically demonstrable skeletal disorders at the craniovertebral angle were asymptomatic.

A feature of lesions of the craniovertebral junction is the poor correlation that exists between the clinicopathological entity and the radiological picture. Gross structural abnormalities such as cavitation of the spinal cord or malformation of the brainstem may not be detectable radiologically, even by the most carefully executed techniques. Conversely, a large proportion of radiological deformities of the craniovertebral junction, particularly skeletal anomalies, are asymptomatic—and therefore probably clinically irrelevant.

List (1941), the American neurosurgeon, must be credited with one of the first attempts to match the clinical and radiological presentation of these lesions. McRae (1960), in a Caldwell Lecture delivered to the American Roentgen Ray Society, discussed the significance of plain-film abnormalities of the craniovertebral junction and emphasized how readily they can be overlooked. He was able to find 38 patients in a Montreal hospice who had been admitted with a diagnosis of multiple sclerosis or cervical disc prolapse—all of whom showed radiological evidence of a local bony lesion below the foramen magnum, to which their symptomatology could be attributed.

This paper is based on analysis of a series of 154 congenital or acquired lesions of the craniovertebral junction encountered over a 12-year period in the Wessex Neurological Centre, Southampton. It was prepared specifically to determine the proportion of such lesions that show no radiological signs, as well as to identify those radiological anomalies which are clinically unimportant.

HINDBRAIN ANOMALY

This diagnosis encompasses a wide spectrum of anomalies which are ill-defined clinically and radiologically, and amenable only to palliative surgery. It includes nowadays more than the classical degrees of congenital hindbrain ectopia described by Chiari (1891), *viz.* type 1—ectopic tonsils only, reaching the C1–2 level; type 2—more complete descent of the hindbrain, including the fourth ventricle. Other entities are: (1) Basilar impression: patients with hindbrain symptoms and signs are encountered, in whom the only detectable abnormality is radiological evidence of basilar impression: X-ray contrast studies and/or neurosurgical exploration reveal a morphologically normal hindbrain. (2) "Basal arachnoiditis", a neurosurgical syndrome of raised intracranial pressure due to hydrocephalus associated with occluded exit foramina and extracranially-situated cerebellar tonsils (Appleby *et al.*, 1969). Presenting often only after middle-age, it may be an acquired syndrome, with the tonsillar malposition due to herniation rather than congenital ectopia. (3) Complicating cord cavitation, arising—according to the theory of Gardner (1965)—in a hindbrain anomaly. In such cases, clinical features of the syringomyelia syndrome may predominate, and clinical or radiological evidence of the hindbrain anomaly may be incomplete or occult.

Table I lists the radiological findings at the craniovertebral angle in 22 patients with verified hindbrain anomalies. Appleby and his colleagues (1968), among others, have verified the absence of plain-film abnormalities in about 50% of patients. Funnelling of the angle—that is, a deformity consisting of an abnormally wide foramen magnum

TABLE I

HINDBRAIN ANOMALY—22 CASES

Plain radiographs:	
funnelled angle	4
coarcted canal	8
basilar impression	7
normal	10 (45%)
Contrast studies:	
tonsillar ectopia	17 (77%)
fat cord	9 (41%)

---

*Lecture delivered at the 150 Academic Festival of the University of Cape Town in December 1979.

combined with widening also of the spinal canal of the atlas and axis vertebrae—is described as the classical plain-film deformity, and the only one typical of hindbrain anomaly (Davies, 1967; Fig. 1); but it is uncommon. Invariable accompaniments of funnelling are a depressed fourth ventricle lying at the level of the foramen magnum, and obstructive hydrocephalus (Fig. 2). A more frequent finding than funnelling is coarctation of the foramen magnum, being usually part of a wider bony anomaly producing basilar impression.

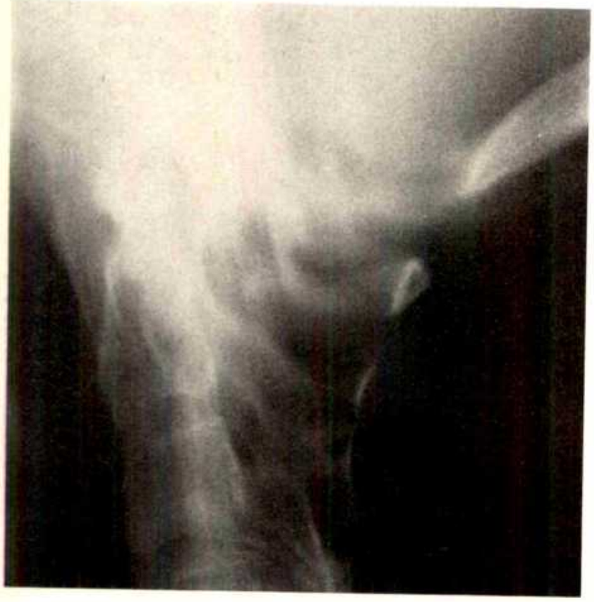


FIG. 1.

Classical funnelling of the craniovertebral angle in a 48-year-old woman with a Chiari type 2 hindbrain anomaly.

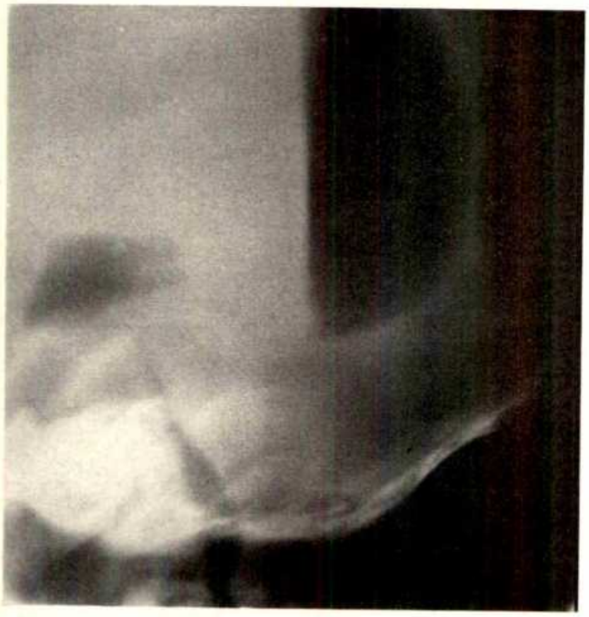


FIG. 2.

A deformed and depressed fourth ventricle and obstructive hydrocephalus, in an infant with a Chiari type 2 hindbrain anomaly.

Basilar Impression

As defined originally by Boogaard (1865, Fig. 3), basilar impression is an invagination or up-turning of the occiput into the skull. The entire circumference of the foramen magnum may be involved, or only a segment (Wackenheim, 1974; Shapiro and

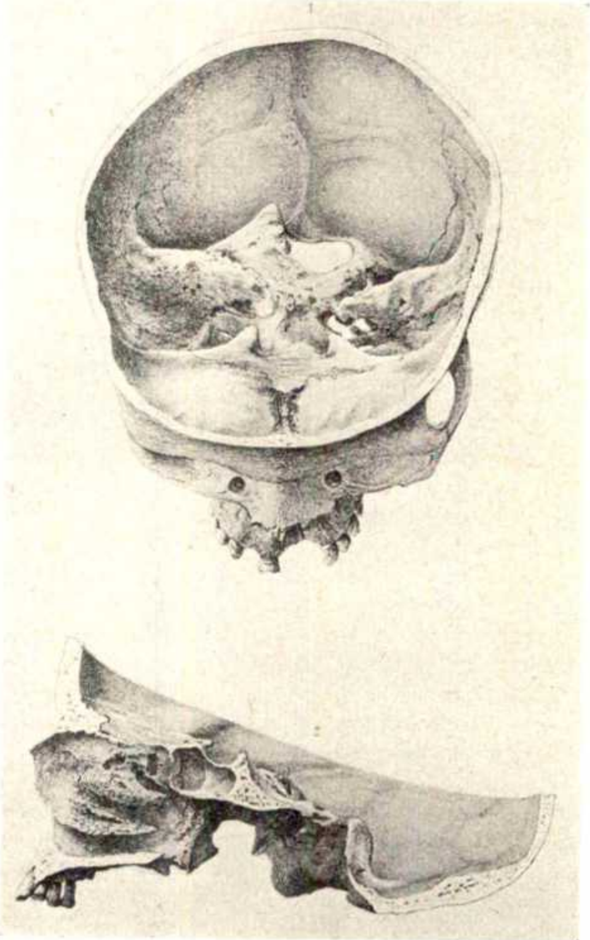


FIG. 3.

Primary basilar impression. One of Boogaard's (1865) original cases, showing asymmetrical upturning of the posterior rim of the foramen magnum. (Reproduced by kind permission of the Editor of the *Nederlands Tijdschrift voor Geneeskunde*).

Robinson, 1976). In the absence of radiological evidence of localized destruction or of a generalized bone-softening process of the vault such as Paget's disease, basilar impression usually has no detectable cause and is thus primary, idiopathic or congenital in nature. Most cases are symptomless (Table II); only the more severe degrees of basilar impression coarct the foramen magnum or upper cervical canal to the extent of causing clinical signs. If combined with hypoplasia of the basisphenoid, the deformity is so great that the clivus-odontoid angle may approximate to 90 deg. (Fig. 4).

Tonsillar ectopia

Extracranially situated cerebellar tonsils usually denote a congenital hindbrain anomaly—*i.e.*, true tonsillar ectopia (Table III)—and this is sometimes associated with cavitation of the spinal cord. Tonsils that are mechanically extruded from the skull as a result of raised intracranial pressure—which is usually caused by neoplastic obstructive hydrocephalus (Fig. 5)—may have appearances identical to tonsillar ectopia. Although ectopic tonsils of the Chiari type 2 malformation are said to be longer and flatter and more tightly plastered against the back of the cervical spinal cord than those in the type 1 variety, reliable differentiation based on the radiomorphology of the tonsils alone is impossible. It must be stressed that the diagnosis of Chiari type 2 malformation depends on the presence of an ectopic fourth ventricle.

TABLE II

BASILAR IMPRESSION—52 CASES

	Asymptomatic
35 primary (congenital, idiopathic)	28
17 secondary to:	
Bone destruction: 3 neoplasms	—
2 infections	—
4 rheumatoid arthritis	1
Bone softening: 3 osteogenesis imperfecta	—
4 Paget's disease	2
1 metabolic	—

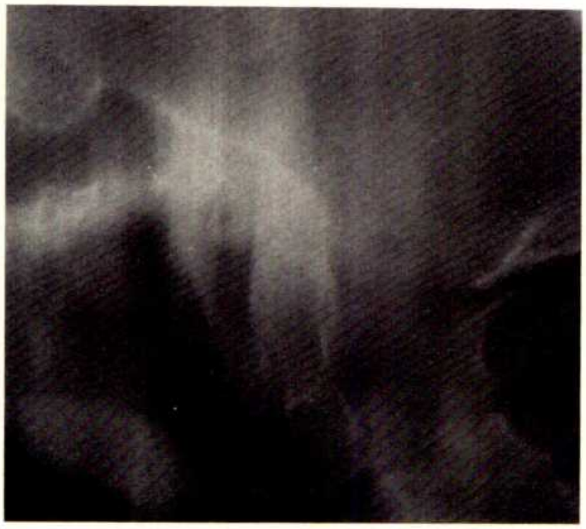


FIG. 4.

Hypoplasia of the basisphenoid causing severe basilar impression. The basal angle is abnormally flat and the clivus-odontoid angle approximates to a right angle: the odontoid process lies within the foramen magnum.

Oil myelography of the craniovertebral angle carried out with the patient supine, a technique perfected by Baker (1963), probably remains the most trustworthy method of demonstrating ectopic or herniated tonsils. Should all tonsils lying beneath the level of the foramen magnum be regarded as abnormal? The majority view is probably Yes, if the tonsils extend significantly below the outer rim of the foramen magnum (Smith and Ridley, 1969; Bloch, Van Rensburg and Danziger, 1974).

Depressed fourth ventricle

Ventriculography remains the most reliable—and possibly the only—way of demonstrating the position of the depressed and deformed fourth ventricle, characteristic of the Chiari type 2 malformation (Fig. 2). Minor degrees of deformity or vertical displacement cannot be reliably identified in the horizontal slices of computed tomography. However, computed tomography will reveal the obstructive hydrocephalus invariably associated with the type 2 malformation, and it will exclude cerebral tumour or other causes of secondary hindbrain herniation. Contrast medium introduced via the spinal theca is usually prevented from entering the fourth ventricle by an associated outlet obstruction.

Outlet arachnoiditis

Arachnoid adhesions in the posterior fossa are a recognized cause of obstructive hydrocephalus not infrequently associated with syringomyelia (McHugh, 1964; Appleby *et al.*, 1969; Logue, 1971). Meningeal infection or haemorrhage at birth or in early life may be responsible, rather than congenital anomaly. Thus the extracranial tonsils often present (Table III) are herniated rather than ectopic. A feature of this condition, differentiating it radiologically from the Chiari type 2 malformation, is the golfball-sized fourth ventricle (Fig. 6).

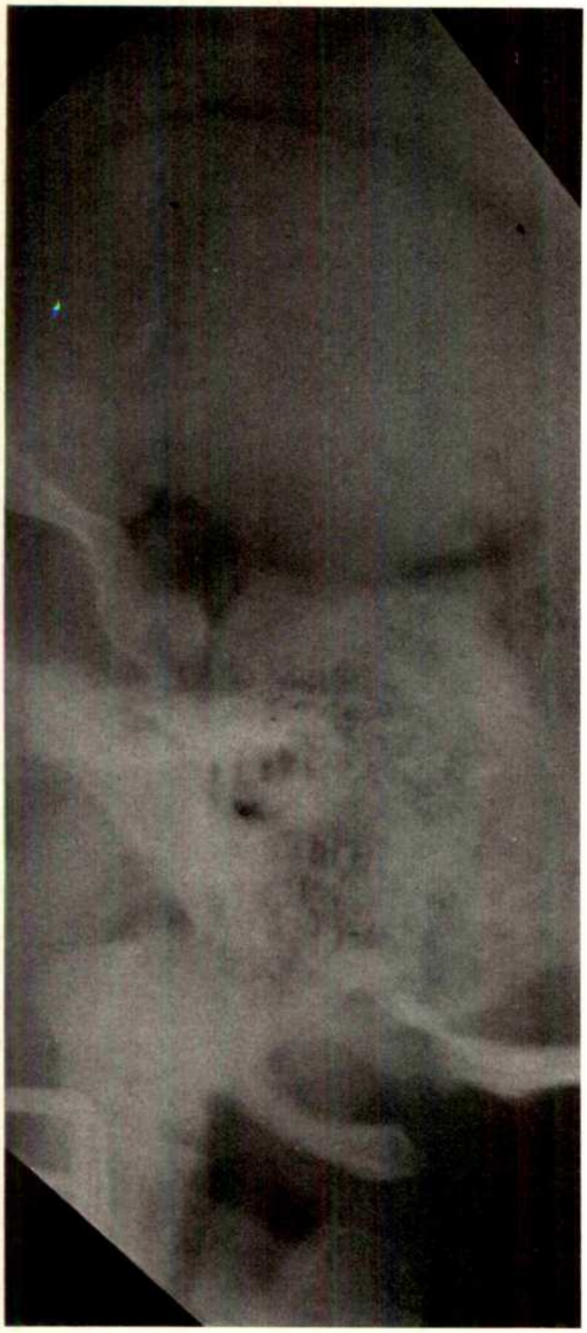


FIG. 5.

Extracranial tonsils demonstrated in the course of a pneumoencephalogram. No gas entered the ventricular system but wideswept pericallosal cisterns were present, indicating enlarged lateral ventricles. Autopsy diagnosis: glioma of the thalamus.

Complicating syringomyelia

Although longitudinal cavitation of the cord is a nosological entity with a well-defined clinical picture, the mechanism of its production is not always clear. Table IV reflects personal experience of the variety of causative mechanisms, as well as the important fact that at least 25% of cases are associated with a hindbrain anomaly. It is possible that the syrinx develops, according to the theory of Gardner (1965), as a complication of the outflow obstruction caused by the ectopic tonsils.

Since the diagnosis of hindbrain anomaly frequently hinges upon demonstrating tonsillar deformity, and since the latter is a sign which is easily

TABLE III

EXTRACRANIAL TONSILS—22 INSTANCES

	Number of cases	Extracranial tonsils
Hindbrain anomaly	22	17
Outlet arachnoiditis	3	3
Brain tumours	12	2

TABLE IV

CORD CAVITATION—37 CASES

Idiopathic syringomyelia	21
Syringomyelia complicating hindbrain anomaly	9
Syrinx associated with:	
– cord neoplasm	1
– Scheuermann's disease	1
– cord trauma	1
– radiotherapy	1
Cystic glioma of cord	2
Non-neoplastic cyst of cord	1

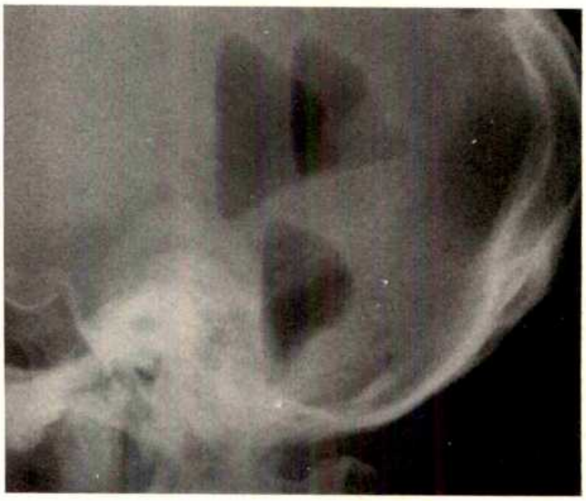


FIG. 6.

Outlet obstruction due to basal arachnoditis in a 61-year-old man. The fourth ventricle, although the size and shape of a golfball, is not displaced from its normal position.

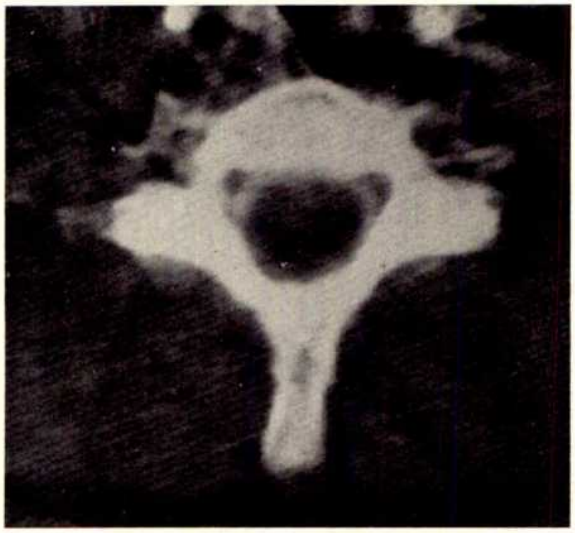


Fig. 7.

Syringomyelic cavitation of the spinal cord revealed by computed tomography following metrizamide myelography.

overlooked by radiologists, some cases labelled as "idiopathic syringomyelia" may actually complicate an obstructing lesion of the craniovertebral angle. Logue (1971) stressed the importance of establishing this connection, since syringomyelic patients may be relieved of their symptoms through surgical decompression of the impacted tonsils.

Radiological evidence of the lesions of syringomyelia may be difficult or impossible to produce, as shown by the following *negative* statistics, based on review of 30 consecutive cases in Southampton: Normal craniovertebral angle and cerebellum—66%; Cervical spinal canal of normal dimensions—63%; Normal spinal cord on myelography—40%. This high incidence of negative findings is caused in part by the dynamic nature of the syrinx, which fills or empties as the patient respectively lowers or raises his head from the horizontal (Bradac, 1972). Computed tomography of the spine, made after intrathecal injection of metrizamide, is probably more reliable than careful myelography in imaging the lesion of syringomyelia (Fig. 7; Forbes and Isherwood, 1978).

Cord Compression

The remaining symptomatic lesions of the craniovertebral junction produce neurological effects by compressing the medulla or upper cervical spinal cord. Most such lesions are acquired, and caused by neoplasm, osteoarthropathy or instability of the atlanto-axial joint. However, congenital coarctation, *i.e.* stenosis of the foramen magnum or upper cervical canal occurring either as an isolated deformity or as part of a more extensive anomaly such as achondroplasia, is an important radiological sign to recognize (Table V). The feature common to this varied group of lesions is compression of neural tissue—either by stenotic deformity of the bony walls (which may be fixed or postural) or a circumscribed space-occupying lesion such as a meningioma. Consequently contrast studies—notably myelography and enhanced computed tomography—may be necessary, in addition to plain radiographs and tomograms, to establish the diagnosis.

TABLE V

Symptomatic compression of the upper cervical cord—40 cases

15 Musculoskeletal disorders:	
atlantoaxial instability	14
atlantoaxial osteoarthritis	1
8 Tumours:	
neurofibroma	4
meningioma	2
metastasis	1
arteriovenous malformation	1
17 Congenital coarctation of the spinal canal:	
foramen magnum	10
C2–3 fusion	4
bony bar	3

Musculoskeletal disorders

Abnormalities of the atlantoaxial joint may cause symptomatic stenosis of the cervical canal. Instability or subluxation, the most frequently encountered abnormality, is usually a complication of rheumatoid arthritis (Fig. 8); it is also seen in Down's syndrome. Separate odontoid process—a radiological differential diagnosis which includes fracture and congenital non-union—is just as likely to cause drop attacks, apnoea under relaxant anaesthesia and other dramatic clinical manifestations, as rheumatoid instability of the atlantoaxial joint. A rare acquired abnormality of this joint, seen in elderly subjects, is a compressive hypertrophic osteoarthropathy (Fig. 9).

Tumours

Six of the eight space-occupying lesions in this group infiltrated or pressure-eroded bone, and plain radiographs revealed them—four neurofibromas, a metastatic deposit and a giant arteriovenous malformation. Three of the neurofibromas widened one or more foramina or eroded the adjacent laminar arch in a characteristic way (Fig. 10). Meningiomas of the foramen magnum usually do not erode bone,

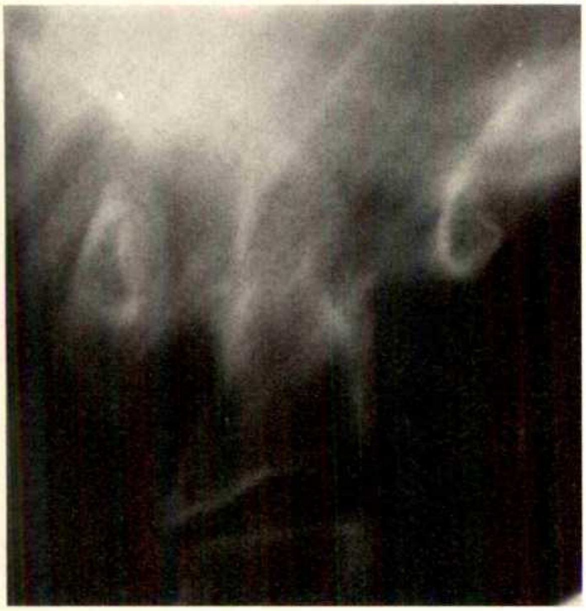


FIG. 8.

Rheumatoid subluxation of the atlanto-axial joint in a 61-year-old patient presenting with signs of cervical-cord compression. Odontoid deformity is the result of grooving by a lax transverse ligament.

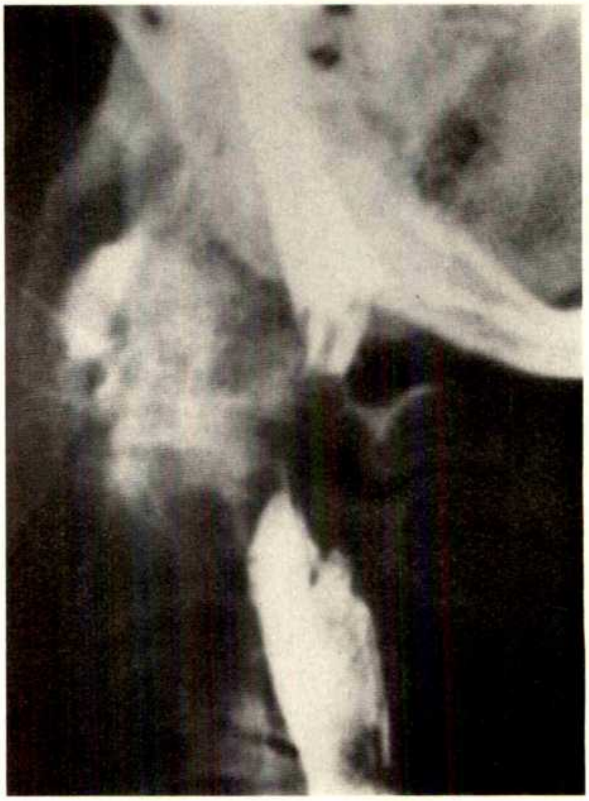


FIG. 9.

Osteoarthritis of the atlanto-axial joint in an 81-year-old man. The hypertrophic changes led to a partial subluxation of the joint which in turn caused severe thecal compression demonstrated by myelography.

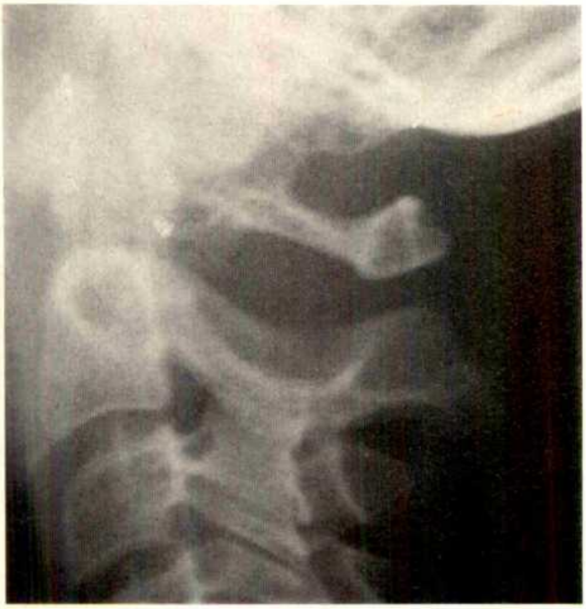


FIG. 10.

Characteristic evidence of dumb-bell neurofibroma: pressure erosion of one half of the upper surface of the laminar arch of the axis vertebra in a 26-year-old woman.

and plain radiographs are therefore unhelpful. These tumours, because of their posterior situation (Fig. 11), are easily missed by inadequate myelography.

Congenital coarctation of the spinal canal

This small but well-defined group of cases comprise two radiological varieties, *viz.* stenosis of the foramen magnum which is usually part of the hindbrain anomaly, and an isolated skeletal anomaly causing symptomatic stenosis of the upper cervical canal such as C2–3 fusion (four out of 23 instances, see Table VI). Three cases were instances of stenosis produced by an anomalous congenital bony bar (Fig. 12).

ASYMPTOMATIC BONY ABNORMALITIES

Table VI lists 139 bony abnormalities of the craniovertebral angle observed in 125 patients in the course of neuroradiological practice over a 12-year period in Southampton. Retrospective examination of the case notes of these patients revealed complaints and clinical signs that were unrelated in 77 of the abnormalities, or 55%. The underlying factor in the production of clinical signs proved to be stenosis of the spinal canal: Table VI shows that those anomalies causing stenosis are less likely to be asymptomatic. Isolated fusion such as atlanto-occipital

TABLE VI

SKELETAL ABNORMALITIES—125 PATIENTS

	Asymptomatic (%)
52 Basilar impression	31 (60)
23 C2-3 fusion	19 (82)
16 Atlanto-occipital fusion	9 (56)
16 Atlantoaxial instability	6 (38)
8 Separate odontoid process	4 (50)
6 Funnelling	3 (50)
6 Coarctation	1 (16)
9 Neurofibroma erosion	1 (11)
3 Multivertebral fusion	3 (100)
139 Lesions	77 (55)

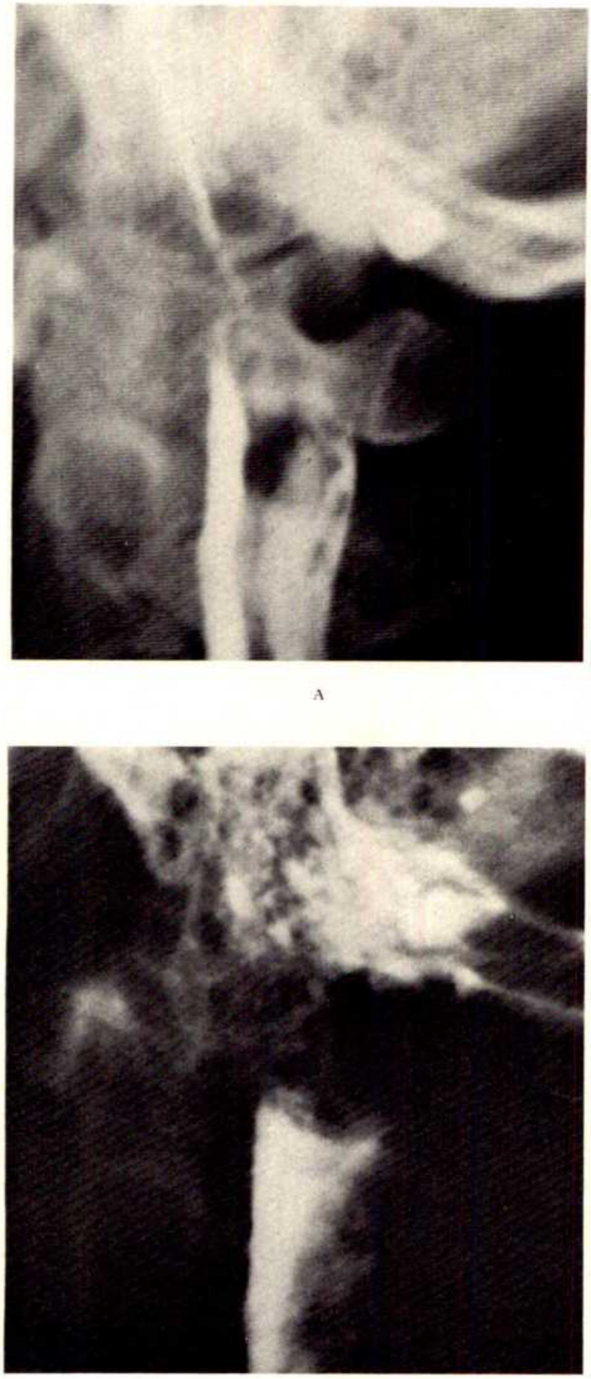


FIG. 11.

Meningioma of the foramen magnum, which intermittently obstructed cerebrospinal fluid flow. A. Oil myelogram, made with the patient prone, proved inadequate to reveal the tumour. B. Repeat examination made a few days later and utilizing the same oil, but with the patient's head turned to one side; the 1.7 cm diameter tumour is satisfactorily outlined.

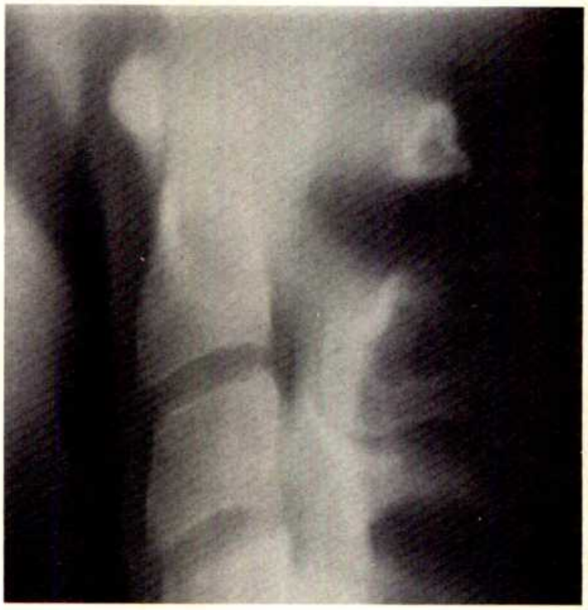


FIG. 12.

Congenital bony bar causing stenosis of the spinal canal. The patient was a 37-year-old man who had been diagnosed six years previously as a case of "atypical multiple sclerosis". Lateral tomogram highlights the additional laminar segment situated between the axis and the third cervical vertebra, which narrows the sagittal diameter of the spinal canal to 7 mm. Good clinical recovery followed operative decompression. This case was reported by Fuller (1970).

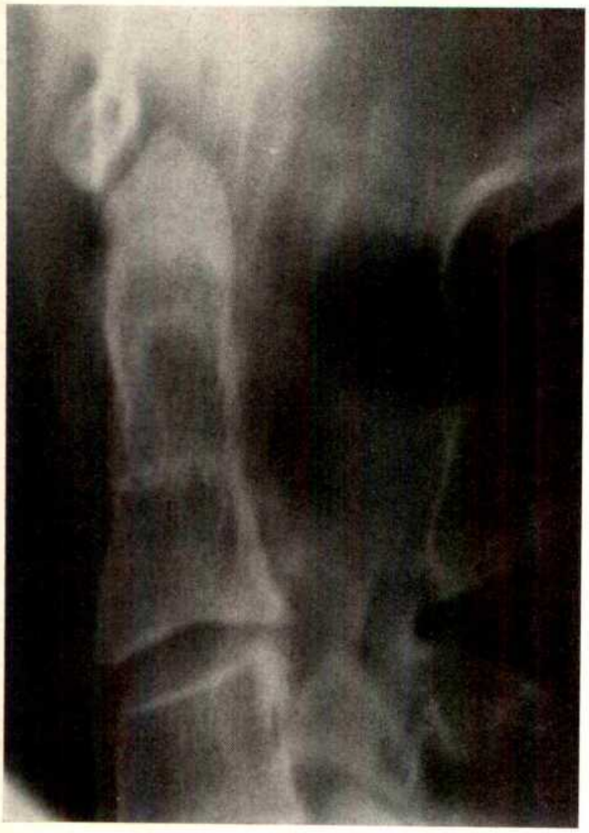


FIG. 13.

Non-significant atlanto-occipital fusion—a chance finding. In the absence of stenosis of the spinal canal, stable fusions at the cranio-vertebral angle are unlikely to be symptomatic.

assimilation, or even bizarre multivertebral deformity, provided it produces no joint instability, is unlikely to cause symptoms (Fig. 13).

REFERENCES

APPLEBY, A., FOSTER, J. B., HANKINSON, J. and HUDGSON, P., 1968. The diagnosis and management of the Chiari anomalies in adult life. *Brain*, *91*, 131–140.

APPLEBY, A., BRADLEY, W. G., FOSTER, J. B., HANKINSON, J. and HUDGSON, P., 1969. Syringomyelia due to chronic arachnoiditis at the foramen magnum. *Journal of the Neurological Sciences*, *8*, 451–464.

BAKER, H. L., Jr. 1963. Myelographic examination of the posterior fossa with positive contrast medium. *Radiology*, *81*, 791–801.

BLOCH, S., VAN RENSBURG, M. J. and DANZIGER, J., 1974. The Arnold-Chiari malformation. *Clinical Radiology*, *25*, 335–341.

BOOGAARD, J. A., 1865. De indrukking der grondvlakte van den schedel door de wervelkolom, hare oorzaken en gevolgen. *Nederlands Tijdschrift voor Geneeskunde*, *2*, 81–108.

BRADAC, G. B., 1972. The value of gas myelography in the diagnosis of syringomyelia. *Neuroradiology*, *4*, 41–45.

CHIARI, H., 1891. Ueber Veränderungen des Kleinhirns in Folge von Hydrocephalie des Grosshirns. *Deutsche Medizinische Wochenschrift*, *17*, 1172–1175.

DAVIES, H. W., 1967. Radiological changes associated with Arnold-Chiari malformation. *British Journal of Radiology*, *40*, 262–269.

FORBES, W. ST. C. and ISHERWOOD, I., 1978. Computed tomography in syringomyelia and the associated Arnold-Chiari type 1 malformation. *Neuroradiology*, *15*, 73–78.

FULLER, D. J., 1970. Surgical relief for spastic tetraplegia due to cervical cord compression. *Journal of Bone and Joint Surgery*, *52B*, 465–467.

GARDNER, W. J., 1965. Hydrodynamic mechanisms of syringomyelia. *Journal of Neurology, Neurosurgery and Psychiatry*, *28*, 247–259.

LIST, C. F., 1941. Neurologic syndromes accompanying developmental anomalies of occipital bone, atlas and axis. *Archives of Neurology and Psychiatry*, *45*, 577–616.

LOGUE, V., 1971. Syringomyelia: a radiodiagnostic and radiotherapeutic saga. *Clinical Radiology*, *22*, 2–16.

MCHUGH, P. R., 1964. Occult hydrocephalus. *Quarterly Journal of Medicine*, *33*, 297–308.

MCRAE, D. L., 1960. The significance of abnormalities of the cervical spine. (Caldwell Lecture). *American Journal of Roentgenology*, *84*, 3–25.

SHAPIRO, R. and ROBINSON, F., 1976. Anomalies of the craniovertebral border. *American Journal of Roentgenology*, *127*, 281–287.

SMITH, J. and RIDLEY, A., 1969. Cerebellar ectopia. *British Medical Journal*, *i*, 353–355.

WACKENHEIM, A., 1974. Roentgen diagnosis of the craniovertebral angle. (Springer Verlag, Heidelberg).

Book review

Science in Action. By J. Lenihan. pp. ix + 223, 1979 (The Institute of Physics, Bristol and London) £7·50.
ISBN 0–85498–035–0

I suppose that the number of physicists who can also call themselves journalists could almost be numbered on the fingers of two hands. Professor Lenihan is one of these and this book contains 65 of his essays, many of which are based on newspaper articles and book reviews which he has written for the non-scientific press over the years. He brings a real breath of fresh air to the subjects he discusses, and to those who know his abilities as a lecturer it will come as no surprise that he treats them with a sense of humour while at the same time getting over with ease the serious points he wants to make. No essay is more than about four pages long and they cover a wide range of topics in chemistry and biology as well as in physics. The feature that they have in common is that they deal with everyday and topical scientific matters of interest to lay reader and scientist alike. There is discussion of the origin of the earth, the possible hazards to health of radio-active fall-out and disco-music, the nuisance of the indestructible plastic bag, the physics of skiing, bicycling and ultrasonics and much more. Do you know who invented the multiplication sign or where Duggan's Dew whisky comes from? You will find the answers in this volume. The pages are delightfully and liberally illustrated with cartoons by Mr. J. B. Fleming which add very much to the enjoyment of the book. This is a most entertaining collection of short articles that show that science is not dull, and as such could be particularly interesting to young people and others who had thought that it was.

N. E. GILLIES.

1981, *British Journal of Radiology*, 54, 203–206 MARCH 1981

Amipaque in coronary angiography and left ventriculography

By D. C. Cumberland, M.B., Ch.B., F.R.C.R.

Department of Radiology, Northern General Hospital, Sheffield

(Received July 1980 and in revised form November 1980)

ABSTRACT

Amipaque (metrizamide) has been directly compared with Urografin and Triosil in coronary angiography and left ventriculography. Amipaque caused significantly less T-wave deflection than either medium when injected into the coronary arteries, and there was a tendency to less reduction in heart rate.

Subjective discomfort was significantly reduced with Amipaque, particularly in left ventriculography.

Amipaque was also directly compared in two concentrations, 370 and 300 mg iodine/ml. There was a slight tendency to less ECG change and subjective discomfort with the lower concentration, and there was no significant reduction in image quality.

The relatively high cost of Amipaque and the necessity of prior mixing make its routine use in adult cardiology unlikely, but it should be valuable in certain cases when minimum toxicity or reduced discomfort are of special importance. A relatively low iodine concentration, for example 300 mg iodine/ml, is sufficient.

Metrizamide (Amipaque, Nyegaard & Co.), a non-ionic low osmolality contrast medium originally introduced for myelography, has been shown by animal experiments to be better tolerated than ionic media in coronary angiography. Almen (1973) found less reduction in heart rate and contractile force while perfusing rabbit coronary arteries with metrizamide than with diatrizoate, iothalamate or metrizamide. Trägårdh *et al.* (1974), using His bundle electrography, found that the injection of metrizamide into the left coronary artery of dogs caused less prolongation of the conduction time through the proximal part of the conducting system than diatrizoate or metrizoate. In 1975, in similar experiments, the same workers showed that metrizamide caused less change in myocardial contractility and aortic pressure.

Clinical trials have confirmed the better tolerance of Amipaque in coronary angiography. Enge *et al.* (1977), comparing Isopaque Coronar (metrizoate) with Amipaque in 30 patients, found that Amipaque caused less reduction in diastolic pressure and less chest pain. There was a tendency to less reduction in heart rate. No difference in the electrocardiogram or angiographic quality was found. Ludwig (1979), in a preliminary report of five patients, showed that 13% of diatrizoate injections caused a reduction in heart rate and blood pressure, against none with metrizamide. Again no difference in image quality or ECG was found.

For an equivalent iodine concentration, metrizamide has an osmolality about one-third that of ionic media. As hyperosmolality is responsible for some of the discomfort caused by contrast media (Björk *et al.*, 1969), metrizamide injections should be better tolerated subjectively. This was the case in the study by Enge *et al.* (1977), Isopaque Coronar (metrizoate) producing greater chest pain and heat sensation than metrizamide.

This study was undertaken to compare two ionic media—Urografin 370 (diatrizoate) and Triosil 370 (metrizoate) with Amipaque in the same concentration, *i.e.* 370 mg iodine/ml, in patients being investigated for ischaemic heart disease. Particular interest was in the ECG changes in coronary angiography and the degree of subjective discomfort in left ventriculography.

Amipaque has also been directly compared in two concentrations, 370 and 300 mg iodine/ml, to determine whether the latter concentration was sufficient for good angiography, and also to detect any possible reduction in ECG changes or subjective discomfort with the lower concentration.

MATERIALS AND METHODS

As in the clinical studies previously mentioned (Enge *et al.*, 1977; Ludwig, 1979), two media were directly compared in each patient. The medium to be injected first was determined by random selection, and thereafter they were injected alternately. The methods of catheterization, data collection and interpretation were similar to a previous trial of coronary angiographic media from this centre (Verel *et al.*, 1975).

A total of 35 patients, all with suspected coronary artery disease, were investigated using Judkins catheters introduced percutaneously by the femoral route. The patients were in three groups, randomly selected as to which pair of media they would receive. Thirteen patients were given Urografin and Amipaque 370, and 11 received Triosil and Amipaque 370. There were 11 patients in the group comparing Amipaque in two concentrations, *i.e.*, 370 and 300 mg iodine/ml. The media being used were unknown to those performing the catheterizations, and when the data were analysed.

The radiological equipment, consisting of the Philips Polydiagnost C with biplane facility, permitted all the angiograms to be performed without any intervening patient movement.

The electrocardiogram was recorded for a few seconds before, during and for 15 seconds after each injection. Further injections and comparisons were not made unless the ECG had returned to its original form for one minute. The pressure at the catheter tip was continuously monitored (except during the injection itself) by strain gauge. Comparisons were not made if the systolic pressure fell below 80 mmHg.

The maximum T-wave deflection was measured after each injection, and any reduction in heart rate of more than five beats/min and lasting for at least three cycles was recorded. All patients had been premedicated with 0.6 mg atropine.

The media were injected by hand at room temperature. The volume injected and the injection times were recorded to ensure that differences in viscosity did not alter the injection characteristics, therefore falsely affecting ECG and other parameters.

Each patient had two left ventriculograms, using the media assigned for the coronary angiograms, in volumes of 45 ml injected by pump at 12 ml/sec.

After each angiogram, whether of the left ventricle or coronary arteries, the patient was asked about the discomfort experienced.

All the films were viewed for angiographic quality, without knowledge of the media used.

Statistical analysis of the coronary angiographic data was by the paired *t* test. In left ventriculography, the comparative discomfort with each medium was analysed by McNemar's test, and the incidence of severe discomfort by the exact probability test of Fisher, Irwin and Yates (two-tailed).

RESULTS

Most patients received six injections into the left coronary artery, thus allowing three comparisons; and two into the right coronary artery. It was found that the parameters measured changed consistently with each pair of injections. For example, if medium "A" gave more T-wave change than medium "B", this trend continued with approximately equal magnitude no matter how many injections were given. Therefore, unlike previous trials, in which each injection has been treated as a separate observation for statistical purposes, the mean value for each parameter produced by each medium in a given patient was determined. This mean value was then regarded as a single observation in order not to give undue statistical significance to the results. If an odd number of injections was given the last reading was discounted, and if there was only one injection into an artery (always the right) this was also discounted, as clearly a comparison could not be made.

None of the differences between the media in coronary angiography, to be described below, can be accounted for by differences in injection volume or rate. Occasionally differences in required injection force were noticed, but these were never regarded as of practical importance, and were not reflected in the injection records. Presumably one automatically adjusts the injection force to give the required image on the television monitor during the cine recording.

T-wave changes in coronary angiography (Fig. 1A–C)

Adequate traces were available in ten patients in each group. Considerably greater T-wave changes were seen with the ionic media than Amipaque. The mean change overall was 9.3 mm with Urografin, 3.9 mm with Amipaque in the first group ($0.001 > p$). The mean change with Triosil was 6.0 mm, against 3.6 mm with Amipaque ($0.01 > p$). There was no significant difference between Amipaque 370 (mean 3.6 mm) and Amipaque 300 (mean 3.7 mm).

Heart rate changes in coronary angiography

In the Urografin/Amipaque group, 12 patients had adequate records for rate assessment. In two, there were mean falls of 6 and 13 beats/min with Urografin, but no change with Amipaque. Ten patients showed no change.

Of 11 patients in the Triosil/Amipaque group, one patient showed a mean fall of 11 beats/min with Triosil but no change with Amipaque. There was no change in the other ten patients.

No instance of rate reduction greater than five beats/min occurred in the Amipaque 370/Amipaque 300 group.

There were no dysrhythmias in any patient.

Subjective discomfort

Ten patients in each group had left ventriculography with both assigned media.

In the Urografin/Amipaque group, six patients experienced less discomfort with Amipaque, none with Urografin ($p=0.02$). Four patients did not describe a difference. Severe discomfort (that is when "very" or "extremely" hot sensation or pain was described) occurred with Urografin in seven patients, with Amipaque in two ($p=0.07$).

In the Triosil/Amipaque group, seven patients preferred Amipaque, none Triosil ($p=0.008$). Severe discomfort occurred with Triosil in eight patients, in two with Amipaque ($p=0.02$).

In the Amipaque 300/Amipaque 370 patients, two preferred Amipaque 300, none the higher concentration. There was no difference in eight. Severe discomfort occurred with Amipaque 300 in two patients, with Amipaque 370 in three patients. The differences in this group are not statistically significant.

If the two ionic media/Amipaque groups are considered together, of 20 patients Amipaque caused less sensation in 13 ($p=0.0001$). Though the difference in incidence of severe discomfort is not statistically significant in the Urografin group alone, that in the Triosil group is, and combining the groups gives a highly significant difference ($p=0.001$). The relative degrees of subjective reaction caused by each medium in the three left ventriculography groups is depicted in Fig. 2.

Detailed analysis of the subjective sensation in coronary angiography is not given as the degree experienced was, as expected, only slight. However, a sensation (usually warmth) was caused by approximately one-half of the injections with the ionic media, compared with one-fifth of the Amipaque injections.

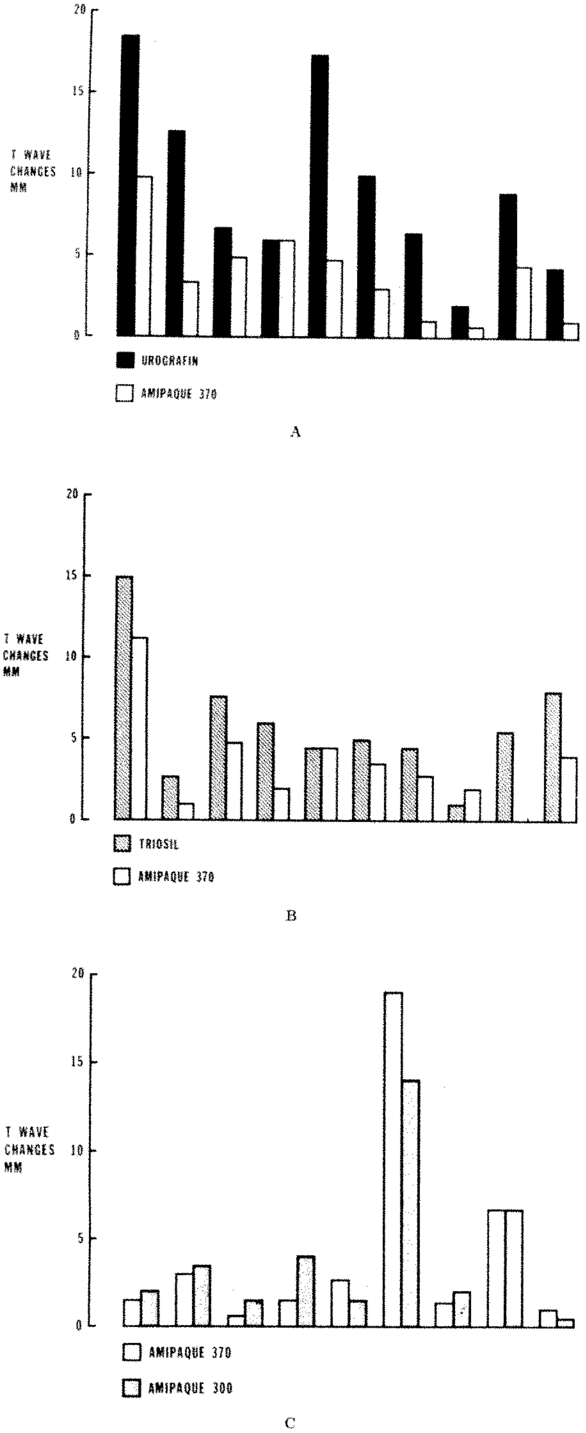


FIG. 1.

(A, B, C) Mean T-wave changes during coronary angiography in three groups of patients, each receiving two contrast media alternately. See Results section for overall means and statistical significance. (One patient in Amipaque 370/Amipaque 300 group had no T-wave change, therefore not included in histogram.)

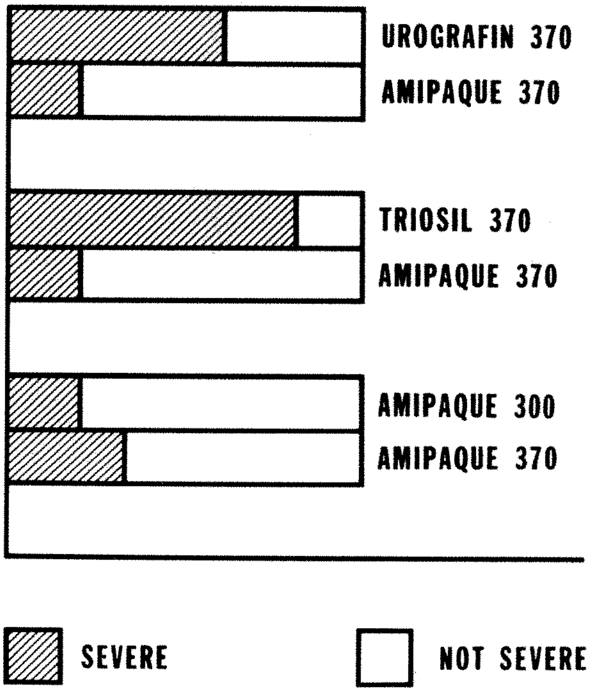


FIG. 2.

Proportion of left ventriculograms associated with "severe" discomfort with each medium in the three groups.

Diagnostic quality

There was no detectable difference in angiographic quality with any of the ventriculograms, nor in coronary angiography between the ionic media and Amipaque. Three of 11 patients had slightly denser coronary angiograms with Amipaque 370 than Amipaque 300 but the difference was not judged to be of any practical importance.

DISCUSSION

Previous trials have not shown any difference between Amipaque and other media in ECG changes (Enge *et al.*, 1977; Ludwig, 1979). This study has, however, revealed consistently less T-wave deflection with Amipaque, this being statistically significant even taking the mean deflection in each patient rather than every coronary injection as an observation. As discussed by Verel *et al.* (1975), the effect on the ECG is widely accepted as an indicator of the myocardial toxicity of a substance injected into the coronary arteries of man. Other techniques, such as the accurate determination of ventricular performance by special pressure recordings or output measurements, are difficult to perform routinely in the clinical setting.

A strictly valid comparison of the T-wave changes produced by Urografin and Triosil cannot be made as they were in different groups of patients, but there was in general less change with Triosil. This conforms to the findings of Verel *et al.* (1975), where a valid comparison was made.

There was a tendency in this trial for Amipaque to cause less decrease in heart rate than the ionic media. Though the differences were not statistically significant, the weight of experimental and clinical evidence (Almen, 1973; Enge *et al.*, 1977; Ludwig, 1979) supports the indication that there is less effect with Amipaque. All the patients in this study had received atropine, which will of course partly mask a tendency to bradycardia, and minor differences in heart rate were not recorded here.

As expected, in view of its relatively low osmolality, Amipaque caused significantly less subjective discomfort than the ionic media. Left ventriculography generally produces less sensation than aortography or limb angiography, and the theoretical expectation of an even more obvious reduction in discomfort with Amipaque is borne out by experience in this centre (to be reported).

There was a slight tendency to less ECG change and subjective discomfort with Amipaque 300 compared with Amipaque 370, but these differences were not statistically significant, and may not be noticeable clinically. The main purpose of using the lower concentration was to determine whether there was any significant reduction in image quality. Though in a few patients slightly better density was noticed in the coronary arteries with Amipaque 370, no loss of diagnostic information occurred with the lower concentration and the difference was not believed to be of practical importance.

Amipaque is relatively expensive and it cannot yet be provided readymade in solution. Its use is therefore probably better restricted to selected cases, for example those patients whose clinical state or history of adverse reaction to coronary angiography demands a medium with minimum toxicity or in whom poor tolerance to discomfort can be predicted. A low iodine concentration, for example 300 mg/ml, is easier to dissolve and of course cheaper.

The advantages of Amipaque in paediatric angiocardiography, where high doses of medium may be used relative to body weight and therefore the systemic consequences of hyperosmolality become important, have been described in another paper (Cumberland, 1981).

ACKNOWLEDGMENTS

My thanks are due to Drs. D. Verel and J. S. Fleming for allowing their patients to be included, and to Drs. I. Glaves, D. Oakley and D. Rickards for performing some of the catheterizations. The ECG technicians, nurses and radiographers provided invaluable help in recording the data. Mrs. K. Windle typed the manuscript and figures.

REFERENCES

ALMEN, T., 1973. Effects of metrizamide and other contrast media on the isolated rabbit heart. *Acta Radiologica, Suppl.* 335, 216–222.

BJÖRK, L., ERIKSSON, V. and INGELMAN, B., 1969. Clinical experience with a new type of contrast medium in peripheral arteriography. *American Journal of Roentgenology, 106*, 418.

CUMBERLAND, D. C., 1981. Metrizamide in paediatric angiocardiography. (In press.)

ENGE, I., NITTER-HAUGE, S., ANDREW, E. and LEVOSTAD, K., 1977. Amipaque: a new contrast medium in coronary angiography. *Radiology, 125*, 317–322.

LUDWIG, J. W., 1979. Use of metrizamide in coronary arteriography. *Diagnostic Imaging, 48*, 223–226.

TRÄGÅRDH, B., BOVE, A. and LYNCH, P., 1974. Cardiac conduction abnormalities during coronary arteriography in dogs. Reduced effects of a new contrast medium. *Investigative Radiology, 9*, 340–345.

TRÄGÅRDH, B., LYNCH, P. and VINCIGUERRA, T., 1975. Effects of metrizamide—a new non-ionic contrast medium—on cardiac function during coronary angiography in the dog. *Radiology, 115*, 59–62.

VEREL, D., WARD, C. and AMAN, M., 1975. Comparison of Triosil 370 with Urografin 76 and Hypaque 65 for coronary arteriography. *British Heart Journal, 37*, 1049–1052.

1981, *British Journal of Radiology*, *54*, 207–211 MARCH 1981

Radionuclide uptake during the evolution of experimental acute osteomyelitis

By *S. H. Norris, F.R.C.S. and †I. Watt, M.R.C.P., F.R.C.R.

Departments of *Orthopaedics and †Radiodiagnosis, Bristol Royal Infirmary, Bristol BS2 8HW

(Received June 1980 and in revised form October 1980)

ABSTRACT

The findings of technetium 99m MDP and gallium 67 citrate scintigraphy are described in the first four days following experimental acute osteomyelitis of the tibia of rabbits. On the day of inoculation, defects in activity are observed in both the perfusion and bone phases of technetium scintigraphy. Similar defects are achieved by saline injection. On subsequent days technetium scintigraphy reveals an increased activity in the perfusion stage but a persisting defect of activity in the bone phase. Gallium activity is increased throughout the period of the study in inoculated animals but not in those injected with saline.

It is concluded that ^{99}Tc^{m} MDP, in its perfusion phase, and ^{67}Ga citrate are highly sensitive indicators of bone inflammation and that early osteomyelitis is characterized by increased activity with these agents together with a technetium bone scan defect.

The aetiology and pathology of acute osteomyelitis is well known (Trueta, 1959). Conventional radiographs are not normally diagnostic early in the disease (Starr, 1922; Hart, 1937) since abnormalities are not usually visualized for at least ten days. Computerized tomography may be of value earlier (Kuhn and Berger, 1979) but the features may not be specific and the technique has a limited availability.

There is mounting evidence that the use of radionuclide scanning may reveal abnormalities many days prior to radiographs (Treves *et al.*, 1976; Letts *et al.*, 1975) and that such examinations may offer an early diagnosis in the clinically obscure case (Gilday and Paul, 1974). However, there are conflicting reports concerning the use of bone scintigraphy in osteomyelitis (Trackler *et al.*, 1976) including false negative bone scans (Russin and Staab, 1976; Garnett *et al.*, 1977) and radionuclide uptake during evolution of the early stages of bone infection is ill understood.

The early evolution of an acute inflammatory lesion of bone has been studied with the two commonly used radiopharmaceuticals, technetium 99m methylene diphosphonate (^{99}Tc^{m} MDP) and gallium 67 citrate (^{67}Ga) both qualitatively and quantitatively. The latter agent, initially described as a malignancy seeking nuclide (Edwards and Hayes, 1970; Winchell *et al.*, 1970), was noted to be useful in the diagnosis of inflammatory lesions (Lavender *et al.*, 1971). Since then it has been routinely employed in pyrexia of unknown origin (Teates and Hunter, 1975) and more specifically to detect bone infection (Rafkin *et al.*, 1974; Handmaker and Giammona, 1976; Lisbona and Rosenthal, 1977; Kolyvas *et al.*, 1978) and spinal infection (Norris *et al.*, 1978 and 1979).

MATERIALS AND METHODS

New Zealand white rabbits were used for the experiment. The animals were immature and weighed 2.0–2.5 kg. A strain of *Staphylococcus aureus* from a patient with acute osteomyelitis was cultured on nutrient agar at 37°C overnight and resuspended in distilled water. The suspension was heated to 100°C for thirty minutes and adjusted to give a final concentration of 10^8 organisms per ml with normal saline. This heat-killed preparation contained no viable bacteria, thereby avoiding contamination of the animal house but providing a potent antigenic stimulus for the duration of the study period (Fisher, 1960). Under general anaesthesia 0.5 ml of this solution together with 0.5 ml sodium morrhuate as a sclerosant were injected directly into the distal medullary cavity of the left tibia using the model described by Norden (1970). Following inoculation sequential scans were obtained. An intravenous dose of 37 MBq ^{99}Tc^{m} MDP was followed by immediate scanning to provide the perfusion image. The bone image was obtained by scanning four hours later. An intravenous dose of ^{67}Ga 9.25–12.95 MBq was followed by an image taken twenty-four hours later. The animals were scanned using a gamma camera with a low-energy collimator for technetium imaging and a medium-energy collimator for gallium.

At the conclusion of the experiments the tibiae were removed from the animals, radiographed, and sectioned to provide histological proof of the inflammatory process. Control animals either received no injection or were injected with normal saline alone.

The scans have been analysed in two ways:

(a) Visual. Images were examined in order to elicit any alteration in normal symmetry between hind limbs. Any disparity was recorded as "hot" indicating increased activity in the infected tibia or "cold" indicating reduced activity compared with the normal contralateral limb.

(b) Computer analysis. Information from the scans was stored in a Link Systems computer. Regions of interest were constructed over the tibiae and a background area between the hind limbs. The mean count rate from each tibial region of interest was expressed as a ratio of left to right, background activity having been subtracted. A ratio above unity therefore represented increased activity in the left tibia.

Three populations of animals were used.

1. *Control group 1*

Four animals received no inoculation and were each scanned on two occasions with ^{99}Tc^{m} MDP at intervals of seven days to assess the reproducibility of the computer ratios.

2. *Control group 2*

Five animals were inoculated with normal saline and scanned with ^{99}Tc^{m} MDP on days 1 and 3, day 1 representing the day of inoculation and on days 2 and 4 with ^{67}Ga.

3. *Study group*

Ten animals were injected with heat killed staphylococci: six were scanned on the same days as control group 2; four animals were scanned with ^{99}Tc^{m} MDP on days 2 and 4 and with ^{67}Ga on days 3 and 5. Hence images with ^{99}Tc^{m} MDP were obtained on each of the four days following inoculation and ^{67}Ga images obtained from the second to fifth days.

RESULTS

1. *Control group 1*

No visible or measurably significant difference was observed between the two sets of scans. (Table I).

2. *Control group 2*

(i) ^{99}*Tc*^{m} *MDP perfusion phase.* No visible or measurable difference was found between scans on days 1 and 3 (Table II). There was a significant fall in activity on day 1, however, when compared to Control group 1, $t=2.44$ $p<0.05$.

(ii) ^{99}*Tc*^{m} *MDP bone phase.* There was again no visible or measurable difference between scans (Table II) but there was a significant fall in activity on day 1 when compared with Control group 1, $t=2.74$ $p<0.02$.

(iii) ^{67}*Ga scans.* No visible or measurable difference between limbs was observed (Table III).

TABLE I

RESULTS OF ^{99}Tc^{m} MDP SCANS IN REPRODUCIBILITY GROUP (FOUR ANIMALS)

	Perfusion		Bone	
	Day 1	Day 7	Day 1	Day 7
Mean	1·05	1·01	1·01	1·05
	p=NS		p=NS	
S.D.	·08	·07	·05	·08
Mean overall	1·02		1·05	
		p=NS		
S.D.	·06		·07	

TABLE II

RESULTS OF ^{99}Tc^{m} MDP SCANS IN CONTROL GROUP (FIVE ANIMALS)

	Perfusion		Bone	
	Day 1	Day 3	Day 1	Day 3
Mean	·86	1·15	·91	1·12
	p=NS		p=NS	
S.D.	·17	·24	·12	·20

TABLE III

RESULTS OF ^{67}GA SCANS IN CONTROL GROUP (FIVE ANIMALS)

	Gallium	
	Day 2	Day 4
Mean	·91	1·03
	p=NS	
S.D.	·06	·23

3. *Study group*

(i) ^{99}*Tc*^{m} *MDP perfusion phase*

(*a*) *Visual analysis.* A cold area in the injected tibia was noticed in every animal on day 1, but this was not marked. On day 2 a rise in local perfusion activity was seen in three out of four animals and on day 3 in all the animals.

(*b*) *Computer analysis.* A fall in activity on day 1 was followed on succeeding days by increased activity (Fig. 2). When these ratios were compared with the mean perfusion ratios in control group 1, significant differences were obtained; day 1, $t=2.79$ $p<0.02$, day 2, $t=3.23$ $p<0.02$, day 3, $t=4.13$ $p<0.01$. The fall in activity on day 1 was no greater than that observed in saline injected controls.

(*ii*) ^{99}*Tc*^{m} *MDP bone phase*

(*a*) *Visual analysis.* This revealed cold areas in the left tibia in all, seen from day 1 throughout the experiment, although with time the cold area became less obvious (Fig. 1B).

(*b*) *Computer analysis.* Ratios were less than unity on day 1 (Fig. 3) and on succeeding days although

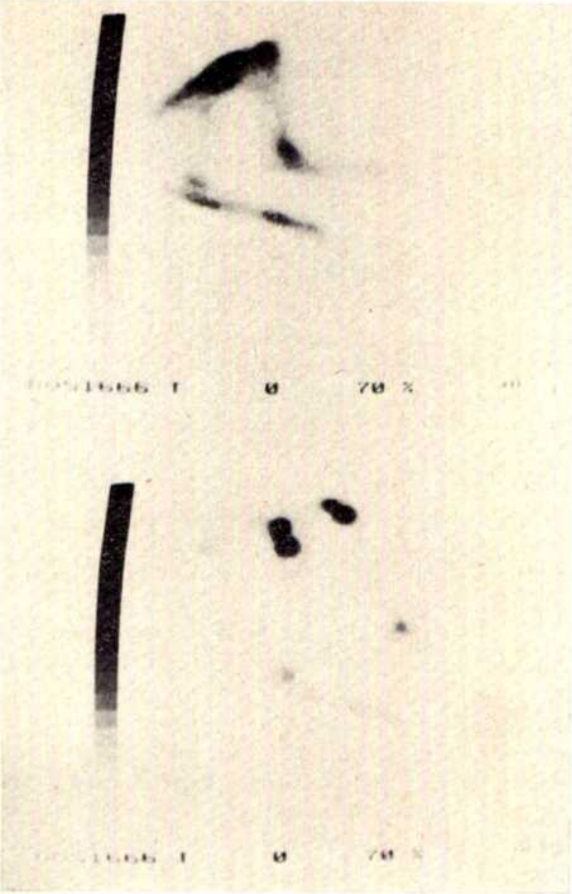


FIG. 1.

(A) ^{99}Tc^{m} MDP perfusion phase in rabbit inoculated with staphylococci, showing increased activity in the distal tibial metaphysis (seen to the right).

(B) ^{99}Tc^{m} MDP bone phase in same rabbit revealing no increased activity in the inoculated tibia.

the level of activity in the left tibia did tend to rise with time. When these ratios were compared with the mean ratio in control group 1, statistically significant differences were noticed on days 1 and 3, $t=5.63$ $p<0.001$ and $t=2.41$ $p<0.05$ respectively. The fall in activity on day 1 was greater than that observed with saline injection $t=2.82$ $p<0.02$.

(iii) ^{67}*Ga Scans*

(*a*) *Visual analysis.* An obvious rise in activity was noticed in all the animals on day 2, and this rise in activity was seen throughout the experiment in all the animals scanned (Fig. 4).

(*b*) *Computer analysis.* An immediate rise in the ratio was seen on day 2 and the local ^{67}Ga activity in the injected tibia tended to increase until day 4. (Fig. 5). The increase in activity was statistically significantly different from the control group.

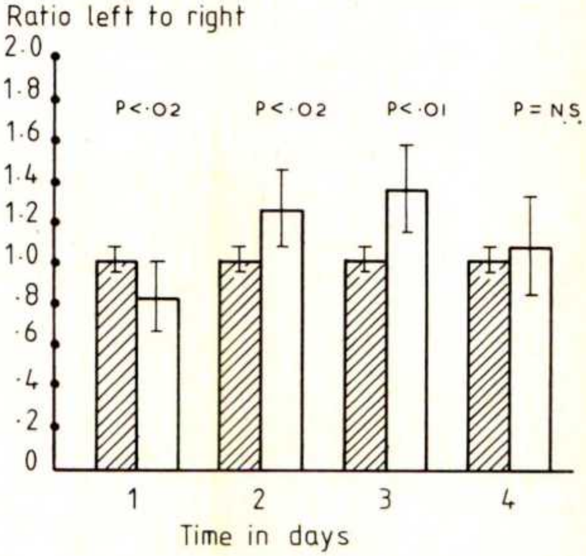


FIG. 2.

Comparison between ^{99}Tc^{m} MDP perfusion scan in experimental groups and mean overall ratios in the control (reproducibility) group (hatched) (mean and 1SD marked).

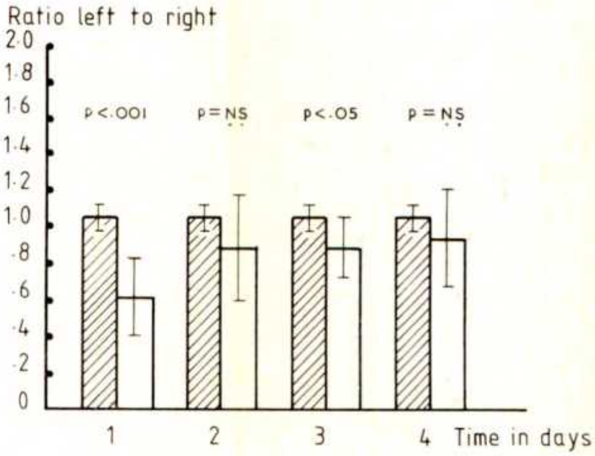


FIG. 3.

Comparison between ^{99}Tc^{m} MDP bone scans in experimental group and mean overall bone scan ratios in control (reproducibility) group (hatched) (mean and 1SD marked).

Radiographs of the excised tibiae at the end of the experiments revealed no abnormality apart from the track where the needle had penetrated the medullary cavity. Histological examination of the bone confirmed areas of acute inflammation with small areas of bone necrosis. Similar changes were seen in all the tibial sections in the study group, but not in the saline injected tibiae.

DISCUSSION

The study confirms that plain radiographs in histologically proven early inflammatory lesions of bone are normal. However, significant isotopic changes were observed from the day of inoculation.

The diagnostic value of the perfusion image of ^{99}Tc^{m} MDP has been previously largely overlooked in the literature. The majority of workers have concentrated upon the bone phase (Letts *et al.*, 1975; Gelfand and Silverstein, 1977; McKay *et al.*, 1978). The present finding of a perfusion defect on day 1 has not been previously recognized. It is important to appreciate however that this defect is non-specific since it could also be induced by saline injection. The subsequent increase in activity was not associated with a bone phase active focus during the study period and this useful sign would go undetected if a perfusion image were to be omitted in the clinical case. Furthermore, previously reported work has suggested that osteomyelitis can be distinguished from soft tissue sepsis by the presence of foci of increased activity at the perfusion phase in both conditions and with an increased focus at bone phase in osteomyelitis but not in cellulitis (Gilday and Paul, 1974; Gilday *et al.*, 1975). However, the present work indicates that this useful discrimination may not be possible in the first few days of infection.

When there is established osteomyelitis ^{99}Tc^{m} MDP in its bone phase usually reveals an increased focus of activity, partly reflecting increased perfusion. The presence of a defect on the bone scan during the first few days of osteomyelitis has not been previously emphasized and may be easily overlooked. This sign is non-specific however, since on the first day of inoculation this can be produced by saline injection but its severity and persistence on subsequent days indicate inflammation. The absence of an increased focus of activity in the experimental situation has been noted previously (Rinsky *et al.*, 1977). In that study 21 of 23 animals scanned in the bone phase on the third day after inoculation showed either a decrease in activity or apparent normality. Hence although increased activity should be noted usually in clinical osteomyelitis it is clearly a reflection of time from inoculation and may also be a feature of osteomyelitis in which there is an appreciable necrotic element accounting for reports of decreased activity in this condition (Duszynski *et al.*, 1975; Russin and Staab, 1976; Garnett *et al.*, 1977), and perfusion and bone phase defects in acute bone infarction (Majd, 1977).

There is no doubt that ^{67}Ga has proved a very desirable isotope in the diagnosis and management of acute bone sepsis. It has been previously noted that ^{67}Ga scans can be abnormal within hours of infection (Rafkin *et al.*, 1974; Deysine *et al.*, 1975a; 1975b; Dye *et al.*, 1979) both experimentally and in the chronic and post-operative situation. The present study has confirmed this suggestion with increased foci of activity being obtained at the

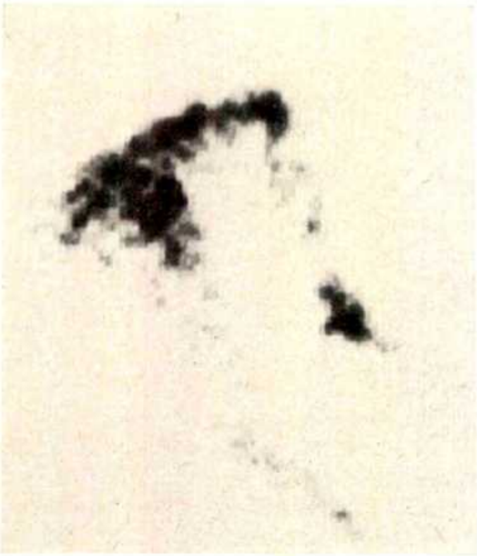


FIG. 4.

^{67}Ga scan of the hind limbs of a rabbit at twenty-four hours from inoculation with staphylococci. There is a well marked increase in activity in the distal left tibia (seen to the right).

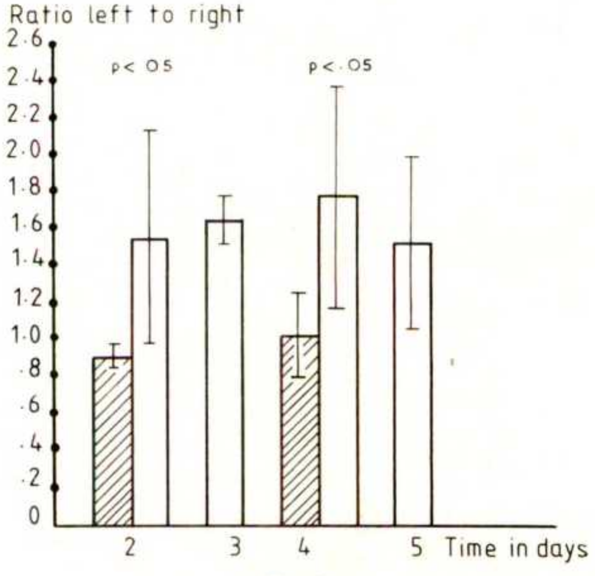


FIG. 5.

Comparison between ^{67}Ga scans in experimental group and control (saline injected group) (hatched) (mean and 1SD marked).

earliest possible time and remaining consistently abnormal on subsequent days. However, ^{67}Ga has major disadvantages including the relatively long half life of seventy-two hours, cost, availability (often having to be ordered in advance) and the necessity to inject the agent the day before imaging can be performed. It should be reserved therefore, for the difficult or unusual clinical problem. ^{99}Tc^{m} MDP, being both cheap and readily available, is of great value in the routine case provided that both perfusion and delayed images are recorded and that its limitations in the early phases of the disease are recognized.

ACKNOWLEDGMENTS

This work was supported by a grant from the Peel Medical Trust.

The authors wish to thank the Bristol Bone Tumour Registry for histological work; Dr. Rosemary Simpson for bacteriological assistance; Dr. Penny Hill for radiopharmaceuticals; Dr. R. Slack for practical help; Mr. A. H. C. Ratliff and Dr. J. Roylance for their advice in the preparation of the manuscript and Mr. E. Turnbull for art work.

REFERENCES

Deysine, M., Rafkin, H., Russell, R., Teicher, I. and Aufses, A. H., 1975a. The detection of acute experimental osteomyelitis with 67-Ga citrate scannings. *Surgery, Gynecology and Obstetrics*, *141*, 40–42.

Deysine, M., Rafkin, H., Teicher, I., Silver, L., Robinson, R., Manly, J. and Aufses, A. H., 1975b. Diagnosis of chronic and post-operative osteomyelitis with gallium 67 citrate scans. *American Journal of Surgery*, *129*, 632–635.

Duszynski, D. O., Kuhn, J. A., Afshani, E. and Riddlesburger, M. M., 1975. Early radionuclide diagnosis of acute osteomyelitis. *Radiology*, *117*, 337–340.

Dye, S. F., Lull, R. J., McAuley, R. J., Van Dam, B. E. and Young, W., 1979. Time sequence of bone and gallium changes in acute osteomyelitis: an animal model (*Abstract*). *Journal of Nuclear Medicine*, *20*, 647.

Edwards, C. L. and Hayes, R. L., 1970. Scanning malignant neoplasms with gallium^{67}. *Journal of the American Medical Association*, *212*, 1182–1190.

Fisher, S., 1960. A heat stable protective staphylococcal antigen. *Australian Journal of Experimental Biology and Medical Science*, *38*, 479–485.

Garnett, E. S., Cockshott, W. P. and Jacobs, J., 1977. Classical acute osteomyelitis with negative bone scan. *British Journal of Radiology*, *50*, 757–760.

Gelfand, M. J. and Silberstein, E. E., 1977. Radionuclide imaging. Use in diagnosis of osteomyelitis in children. *Journal of the American Medical Association*, *237*, 245–247.

Gilday, D. L. and Paul, D. J., 1974. The differentiation of osteomyelitis and cellulitis in children using a combined blood pool and bone scan (*Abstract*). *Journal of Nuclear Medicine*, *15*, 494.

Gilday, D. L., Paul, D. J. and Paterson, J., 1975. Diagnosis of osteomyelitis in children by blood pool and bone imaging. *Radiology*, *117*, 331–335.

Handmaker, H. and Giammona, S. T., 1976. The "hot-joint" increased diagnostic accuracy using combined ^{99m}Tc-phosphate and ^{67}Ga citrate imaging in paediatrics (*Abstract*). *Journal of Nuclear Medicine*, *17*, 554.

Hart, V. L., 1937. Acute haematogenous osteomyelitis in children. *Journal of the American Medical Association*, *108*, 524–528.

Kolyvas, E., Rosenthall, L., Ahronheim, G. A., Lisbona, R. and Marks, M. I., 1978. Serial Ga-67 scanning during treatment of acute osteomyelitis in children. *Clinical Nuclear Medicine*, *3*, 461–466.

Kuhn, J. P. and Berger, P. E., 1979. Computed tomographic diagnosis of osteomyelitis. *Radiology*, *130*, 503–506.

Lavender, J. P., Lowe, J., Barker, J. R. and Burns, J. I., 1971. Gallium-67 citrate scanning in neoplastic and inflammatory lesions. *British Journal of Radiology*, *44*, 361–366.

Letts, R. M., Afifi, A. and Sutherland, J. B., 1975. Technetium bone scanning as an aid to the diagnosis of atypical acute osteomyelitis in children. *Surgery, Gynecology and Obstetrics*, *140*, 899–902.

Lisbona, R. and Rosenthall, L., 1977. Observations on the sequential use of ^{99m}Tc-phosphate complex and ^{67}Ga imaging in osteomyelitis, cellulitis and septic arthritis. *Radiology*, *123*, 123–129.

McKay, W. J., Andrews, J. T. and Thomas, D. P., 1978. The value of the bone scan in the early diagnosis of infective skeletal pathology. *Australasian Radiology*, *22*, 165–169.

Majd, M., 1977. Radionuclide imaging in early detection of childhood osteomyelitis and its differentiation from cellulitis and bone infarction. *Annals of Radiology*, *20*, 9–18.

Norden, C. W., 1970. Experimental osteomyelitis. I. A description of the model. *Journal of Infectious Disease*, *122*, 410–418.

Norris, S. H., Ehrlich, M. G., Keim, D. E., Guiterman, H. and McKusick, K. A., 1978. Early diagnosis of disc space infection using gallium^{67}. *Journal of Nuclear Medicine*, *19*, 384–386.

Norris, S. H., Ehrlich, M. G., McKusick, K. and Provine, H., 1979. The radioisotopic study of an experimental model of disc space infection (*Abstract*). *Journal of Bone and Joint Surgery*, *60-B*, 281.

Rafkin, H., Deysine, M., Teicher, I., Russell, R. and Aufses, A. H., 1974. Detection of experimental osteomyelitis with gallium-67 citrate. *Surgical Forum*, *25*, 485–487.

Rinsky, L., Goris, M. L., Schurman, D. J. and Nagel, D. A., 1977. ^{99}Tc bone scanning in experimental osteomyelitis. *Clinical Orthopaedics and Related Research*, *128*, 361–366.

Russin, L. D. and Staab, E. V., 1976. Unusual bone scan findings in acute osteomyelitis. Case report. *Journal of Nuclear Medicine*, *17*, 617–619.

Starr, C. L., 1922. Acute haematogenous osteomyelitis. *Archives of Surgery*, *4*, 567–587.

Teates, C. D. and Hunter, J. G., 1975. Gallium scanning as a screening test for inflammatory lesions. *Radiology*, *116*, 383–387.

Trackler, R. T., Miller, K. E., Sutherland, D. H. and Chadwick, D. L., 1976. Childhood pelvic osteomyelitis presenting as a cold lesion on bone scan. *Journal of Nuclear Medicine*, *17*, 619–622.

Treves, S., Khettry, J., Broker, F. H., Wilkinson, R. H. and Watts, H., 1976. Osteomyelitis: early scintigraphic detection in children. *Pediatrics*, *57*, 173–186.

Trueta, J., 1959. The three types of acute haematogenous osteomyelitis. *Journal of Bone and Joint Surgery*, *41-B*, 671–680.

Winchell, H. S., Sanchez, P. D., Watanabe, C. K., Hollander, L., Anger, H. O., McRea, J., Hayes, R. L. and Edwards, C. L., 1970. Visualization of tumours in humans using ^{67}Ga citrate and the Anger whole body scanner, scintillation camera and tomographic scanner. *Journal of Nuclear Medicine*, *11*, 459–466.

1981, *British Journal of Radiology*, 54, 212–220

Mammographic practice and dosimetry in Britain

By M. Fitzgerald, B.Sc., M.Sc., D. R. White, M.Sc., Ph.D., *E. White, M.R.C.P., F.R.C.R. and *†J. Young, B.M., B.Ch.,F .R.C.R.

Departments of Radiation Physics and *Diagnostic Radiology, St. Bartholomew's Hospital, London EC1A 7BE

(Received March 1979 and in revised form September 1980).

Abstract

A survey of mammographic techniques and dosimetry in 61 NHS centres in Britain has been completed. Physical parameters measured at each centre included tube output, half-value thickness, peak kilovoltage, surface dose and percentage depth dose. Ionisation and thermoluminescence dosimetry were employed and image quality was assessed subjectively using a test phantom. Absorbed doses are given at the plane surface of an average-sized, 5 cm thick, homogenous breast composed of 50% fat and 50% water. The doses fall naturally into the four combinations of molybdenum (Mo) and tungsten (W) targets and film (F) and xerox (X) receptors. The Mo/X group produced the best images of the phantom but also the highest mean dose of 3.26 cGy (rad) for a cranio-caudad (c-c) view and its use does not seem justified for asymptomatic screening. The Mo/Lo-Dose or MIN-R film combination gave a mean dose of 0.95 cGy(rad) for a c-c view whereas the W/X group gave 0.89 cGy(rad) and superior image quality. The W/F group gave the poorest image quality and its continued use for mammography is questionable.

The possibility of including mammography in a screening programme for breast cancer necessarily involves discussion of the balance between the benefit and the risk (Bailar, 1976). A survey was organized under the auspices of the Hospital Physicists' Association to provide information on the radiation doses involved. Many of the National Health Service hospitals undertaking mammography in England, Scotland and Wales were visited.

The aim was to record details of the X-ray equipment, technique, the number of patients and the range of exposure factors used. The physical measurements were of tube output, half-value thickness (HVT), peak kilovoltage, surface dose and % depth dose and an assessment was made of image quality using a suitable test object. Measurements were done at the average exposure factors for each centre. The survey, conducted during the period July 1976 to June 1977, required the co-operation of eight medical physics departments throughout Britain. To ensure that the measurements were performed in a standard manner, two identical sets of measuring equipment were constructed and distributed to the departments concerned.

Physical Measurements

Five physical parameters were considered for the survey.

1. *Tube output (air kerma)*

This was measured using one of two 35 cc ionization chambers (Pitman Ltd.) supplied with the equipment, coupled to the electrometer (37C or 37D) belonging to the participating physics centre. For machines having automatic exposure-control (AEC) a 5 cm thick breast phantom was positioned in the beam so that a representative radiographic exposure was given. A suitable electrical current source and a 518 MBq (14 mCi) ^{241}Am point source (59.5 keV γ-ray emission) were provided so that the correct functioning of the electrometer and chamber could be checked before use. The mean of the current source readings for each physics department was used to correct the readings for electrometer sensitivity. The chamber responses were checked at various X-ray qualities against a secondary standard Grenz-ray chamber calibrated at the National Physical Laboratory.

2. *Half-value thickness*

This was measured in aluminium using the 35 cc chamber and a lead diaphragm to define the beam size. Many of the "specialized" mammography units utilized a short FSD (<40 cm) and compression cones with Perspex windows. These had to be removed to accommodate the apparatus but the total beam filtration was maintained by the addition of a suitable thickness of Perspex. The expected accuracy is within ± 0.05 mm Al.

3. *Peak kilovoltage*

A penetrameter was used which conformed closely to published design suggestions (HPA, 1976) and

---

Special note
This study was instigated by the Diagnostic Radiology Topic Group of the Hospital Physicists' Association under the chairmanships of Dr. J. Law, Mr. E. T. Henshaw and Dr. B. L. Reece and was partly funded by the Department of Health and Social Security. Certain of the measurements were undertaken by the following physicists (and members of their Departments): Mr. M. A. Bullen, Mr. B. E. Keane, Mr. J. Kennedy, Mr. E. T. Henshaw, Dr. B. M. Moores, Dr. B. L. Reece and Mr. A. Robinson.

†Present address: Medical University of South Carolina, Charlestown, S. Carolina, USA.

was calibrated by the NPL. Kodak RP54 film was used which was developed on site. It has been shown (HPA, 1976) that no corrections are necessary for the effects of different development conditions or, at the kilovoltage used (maximum measured—49 kV), of different voltage waveforms. None have been applied for differences in target and filtration and the expected accuracy is within ±2 kV.

4. *Surface dose and percentage depth dose*

Surface doses were calculated from the measurements of air kerma and were also measured directly using lithium fluoride ribbon dosemeters. The ribbons were used with an epoxy-resin phantom (White *et al.*, 1977) representing 50% fat/50% water by weight, which is thought to be a reasonable compromise between the essentially glandular tissue of the younger breast and the essentially fatty tissue of the older breast. Recent elemental analyses of mastectomy specimens (Hammerstein *et al.*, 1979) appear to confirm the suitability of this choice. Between 10 and 50 keV the radiation characteristics of the chosen substitute material were within 5% of those calculated for the tissue.

The dosimetry phantom consisted of a stack of up to six D-shaped slabs, each 1 cm thick and of surface area 93 cm^2 on each side. Ribbons were accommodated in recesses in each of the six slabs. Extensive calibrations were carried out against suitable secondary standard ionization chambers over a range of X-ray beam qualities using both molybdenum and tungsten target tubes and traceable to the National Physical Laboratory. The response relative to ^{60}Co γ-rays showed reasonable agreement with published results (Ruden, 1976; Hammerstein *et al.*, 1979). A calibration was also provided at the Memorial Hospital, New York, which was traceable to the National Bureau of Standards, and gave agreement within 4% at 30 kV. Each ribbon was numerically identified and an individual response correction was applied.

The absorbed dose, D, at the surface of the breast phantom was obtained from the air kerma, K, using the relation $D=K.B.F$, where B is the backscatter factor (adapted from *The British Journal of Radiology* Supplement No. 11, 1972) and F is the factor to convert from air kerma to absorbed dose. The value of F has a limited energy dependence in the range 10 to 50 keV and for practical spectra a value of 0.74 was used which was derived from the work of Hammerstein *et al.* (1979). A nominal correction was introduced for the change in thermoluminescent response with depth in the phantom, the uncertainty of which is estimated to be within ±5%.

5. *Image quality*

This was assessed subjectively using a D-shaped phantom 4 cm thick with a sloping anterior edge and bulk composition the same as for the dosimetry slabs. It contained test pieces representative of the size, shape and composition of water-like and adipose-like structures and calcifications found within the breast. The test pieces were placed 1 cm below one surface so that by inversion of the phantom two object-to-receptor distances (o.r.d.) of 1 cm and 3 cm were provided. Details of the phantom have been given by White and Tucker (1980).

The two views of the phantom were taken using the normal machine settings and imaging methods used at the centre for a cranio-caudad view. Films were developed on site by the radiography staff. The resulting images were assessed by two radiologists (using a variable intensity white light illuminator for films including Agfa Medichrome) and two physicists (using a normal viewing box for films). The assessors were not told of the total number of objects in the phantom, only of their general position. They were instructed to familiarize themselves with the image so as to pre-empt any learning effect and to discount any objects of which they were unsure. The total number of objects discernible in an image was called the "image score", which was used as a measure of image quality. The maximum image score obtainable was 78.

ASSESSMENT OF MAMMOGRAPHIC PRACTICE

A summary of the most important information gathered during the survey appears in Table I. Details have been organized to show the numbers of the various machines, imaging systems and techniques in use during the survey and the figures in brackets give the revised details at May 1978.

Exactly two-thirds of the machines were specialized units and all but one of these had molybdenum targets; of the specialized units, two-thirds were made by CGR or GEC. Film mammography was used exclusively by 76% of the hospitals, xeromammography exclusively by only 16% and a combination of both by the remaining 8%. Only positive development xeromammography was encountered. The different techniques in use, *e.g.* collimation, field size and shape were to some extent a reflection of the configurations of the various purpose-built machines. The choice of imaging method did not seem to be the decisive factor in the choice of X-ray tube or vice-versa; the equipment already installed, the number of patients and financial considerations were probably influential. All but one of the centres used mammography for symptomatic diagnosis and

TABLE I

SUMMARY OF INFORMATION COLLECTED

1. X-ray machine	63 (60) in 61 (58) centres 42 "specialized"; 16 CGR, 12 (13) GEC, 1 IGE, 7 Philips, 5 Siemens, 1 (0) Todd Research Targets: 41 MO, 1 W. 21 (18) "General"; 3 Dean, 5 (3) GEC, 1 GR, 1 IGE, 1 Newton Victor, 2 Philips, 5 (4) Siemens, 3 Watson. Targets: 3 (4) Mo, 18 (14) W.
2. Target/imaging	44 Molybdenum: 37 (36) film, 3 xerox, 4 (5) film + xerox; 19 (16) Tungsten: 11 (8) film, 7 xerox, 1 film + xerox Total film: 53/63 = 84% (83%) Total xerox: 15/63 = 24% (25%) Total film + xerox: 5/63 = 8% (10%) 6 (5) Agfa: 1 (0) D7, 1 (2) Mamoray, MR 50, 4 (3) Medichrome. 23 (17) Du Pont: 23 (17) Lo-Dose. 22 (28) Kodak: 3 (1) Industrex C, 2 (1) Industrex D. 1 (0) Kodirex, 5 (20) MIN-R 2 (1) Multi-pack, 2 X-OMAT MA, 1 X-OMAT, 6 (2) PE4006. Development: 43 automatic, 10 manual Wrapping: 32 vacuum, 20 envelope, 1 plastic cassette.
3. Collimation/ Compression	Cones—50, Light beam diaphragm—19. Compression: Yes = 52, No = 13. Field sizes: smallest—9cm × 12cm, largest—24 cm × 33 cm. Field shape: circular: 4; D-shaped: 33; oval: 1; rectangular: 22; square: 2; trapezoidal: 1.
4. Patient protection	Yes = 25, No = 38
5. Reasons for mammography	Asymptomatic screening: 11; post-radiotherapy: 2; post-surgery: 1; pre-radiotherapy: 23; symptomatic diagnosis: 62.
6. Other diagnostic methods	None: 51; ductograms: 4; thermography: 8; ultrasound: 2.
7. Patient load	1—560 per month; mean = 74.7 per month
8. Number of views	Cranio-caudad only: 2; cranio-caudad + medio-lateral: 53; cranio-caudad + medio-lateral + axillary: 8.

Bracketed figures are revised details for May 1978; Mo = molybdenum, W = tungsten.

ten centres undertook asymptomatic screening, although the percentage of the total number of patients that this represented is not known.

By May 1978 three centres previously relying on general units had ceased mammography and three others had turned to molybdenum tubes; Du Pont Lo-Dose and Kodak MIN-R were used at nine more centres.

RESULTS

Data were obtained for all 63 machines at the usual X-ray settings for the cranio-caudad view of an "average breast" and at the medio-lateral settings if these were different.

The HVT ranged from 0.2 to 1.7 mm Al. With one exception the values of HVT obtained with tungsten-target tubes were all greater than 0.6 mm Al, and those obtained with molybdenum-target tubes were less than 0.6 mm Al, although the kilovoltages ranged from as low as 29 kV for tungsten to as high as 47 kV for molybdenum.

Measured peak kilovoltages ranged from 24 to 49 kV and were generally within a few percent of the set kilovoltage, although 22/107 were more than 10% different, (*i.e.* $\sim$3 to 4 kV) and seven were over 20% higher.

The correspondence between the percentage depth dose and HVT is shown in Fig. 1 which gives the depths at which the dose was reduced to 50% and 10% of that at the surface. These depths were for molybdenum (with 2/55 exceptions) $\leq$1.2 cm and $\leq$3.8 cm respectively, whereas for tungsten the corresponding values were $\geq$1.2 cm and $\geq$4.6 cm respectively. These results are in fair agreement with those of Boag *et al.* (1976).

The variation in exit percentage depth dose with half-value thickness for a 5 cm thick breast is demonstrated in Fig. 2; the distinction between molybdenum and tungsten targets is apparent. For molybdenum the exit percentage depth dose was (with two exceptions) $\leq$6.6% (lowest 1.0%), whereas for tungsten the value was $\geq$8.3% (highest

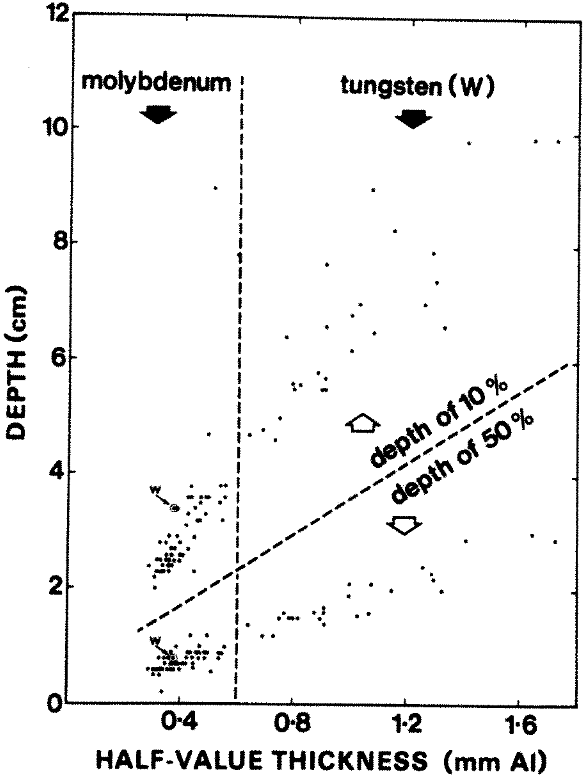


FIG. 1.

Depths at which the surface absorbed dose was reduced to 50% and 10% as a function of X-ray beam quality.

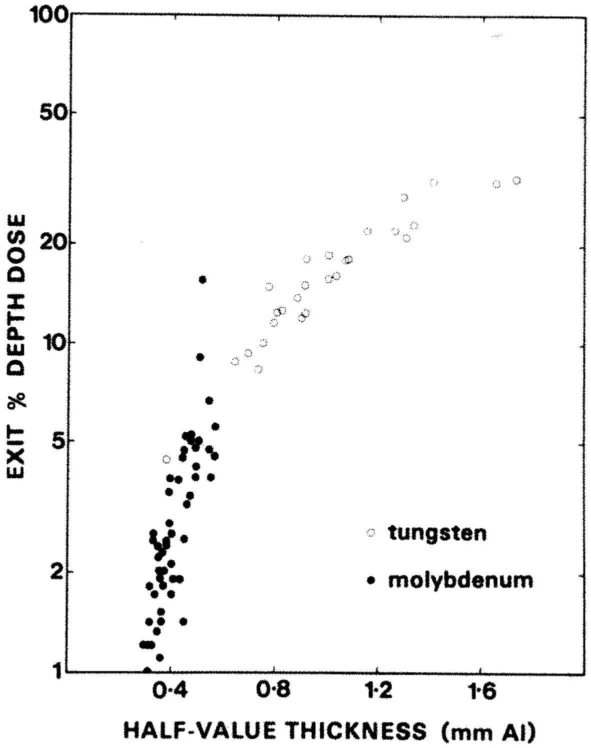


FIG. 2.

Exit plane (5 cm) percentage depth dose as a function of X-ray beam quality.

32.0%). The dependence of percentage depth dose on half-value thickness with molybdenum targets is fairly steep. Mean percentage depth-dose curves are presented in Fig. 3. The spread in results apparent in Figs. 1 to 3 may be due partly to differences in kilovoltage, FSD, waveform and filtration.

The significance of the image scores was tested by analyses of variance of the mean scores. Two groups of images were studied, namely the 76 sets of film results and the 21 sets of xerox results. Mean scores and their statistical significance are given in Table II. With one exception, the scores from the four observers were significantly different from each other for both xerox and film, but only with film were the scores significantly higher when the test objects were closer to the receptor. When considered together, the physicists' scores of the xeromammograms were significantly higher than those of the radiologists; the reverse was true with films.

Cranio-caudad view

Since the majority of results were for the cranio-caudad view these will now be considered. The

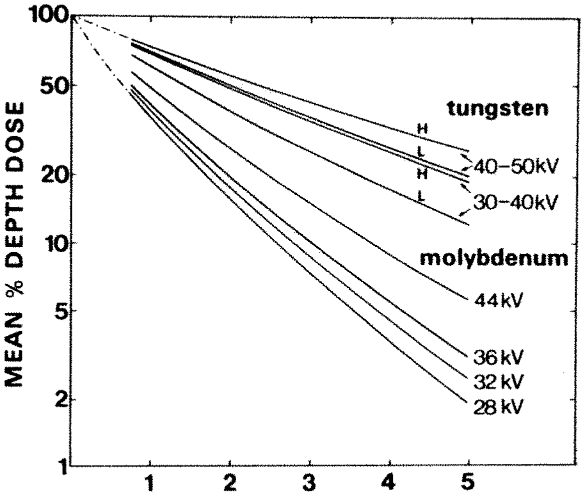


FIG. 3.

Mean percentage depth dose curves for tungsten and molybdenum targets at various kilovoltages. (H = high filtration, 1.7 to 2.8 mm Al; L = low filtration, 0.5 to 1.5 mm Al).

means of the scores attributed by the observers to each of the 11 object types for both film and xerox images are listed in Table III. Those of the xeromammograms were equal to or higher than those of the films for each of the 11 object types for both values of o.r.d. and were noticeably higher for adipose filaments and cubes, aluminium oxide spheres and the smaller silicon cubes. The one exception was skin, for which film gained a higher mean score than xerox at 1 cm o.r.d. On films, the adipose and water filaments and cubes were discernible only rarely. On xeromammograms also these cubes proved very difficult to see, but over 75% of adipose filaments were seen in nine of the 15 images. Also, 94% of the aluminium oxide spheres were seen on all but one of the xeromammograms, whereas on the corresponding films the number seen ranged from 69% to 100% of the maximum obtainable.

Mean surface doses and image scores and their ranges are presented in Table IV for different target and receptor combinations. The dose results must be judged in relation to the image information and the following conclusions can be drawn from this table:

(a) Xerox/molybdenum gave the highest score, but also by far the highest surface dose. With a tungsten target, the score was reduced by only 4% but the dose was reduced by a factor of 3.7 (3.26 to 0.89 cGy (rad)).

TABLE II

Mean image scores and the statistical significance of their differences

Condition	Mean film scores*	Mean xerox scores*
1 cm object to receptor distance† 3 cm object to receptor distance†	32.2 31.5 } $p < 0.01$	39.0 37.9 } not significant
Observer 1‡ Observer 2‡ Observer 3‡ Observer 4‡	32.8 25.6 36.8 31.4 } $p \leq 0.001$ §	40.0 40.0 42.1 31.7 } $p < 0.001$
Physicists (observers 1 + 2)‡ Radiologists (observers 3 + 4)‡	29.2 33.8 } $p < 0.001$	40.0 36.9 } $p < 0.01$

*Mean values above refer to all the film and xerox assessments; those stated later refer to only the 67 cranio-caudad views.
†Mean scores for observers 1 to 4.
‡Mean of scores for 1 cm and 3 cm object to receptor distances.
§Except between observers 1 and 4 for which $p < 0.05$.

TABLE III

Mean image scores for each of the 11 phantom details for 1cm and 3cm object to receptor distances

	Skin	Adipose filaments	Aluminium oxide spheres	Water filaments	Adipose cubes	Water cubes	Water cylinders	Adipose cylinders	Silicon cubes, 0.05 to 0.35 mm	Silicon filaments	Silicon cubes, 0.30 to 0.05 mm
Maximum	9	4	8	4	8	8	7	7	8	7	8
Film	5.0	0.0	7.0	0.9	0.0	0.1	5.4	4.5	2.1	5.6	1.2
1 cm o.r.d.											
Xerox	4.7	2.8	7.7	1.2	1.0	0.3	6.3	5.1	2.7	6.0	3.0
Film	4.2	0.0	6.9	0.9	0.0	0.1	5.4	4.5	1.9	5.6	1.3
3 cm o.r.d.											
Xerox	4.6	2.2	7.9	1.6	0.5	0.4	6.1	5.1	2.8	5.8	2.9

(b) Molybdenum/film required twice the surface dose that tungsten/film did, but the image score was 34% higher.

(c) Molybdenum/film gave a 30% higher surface dose than tungsten/xerox.

These doses were averaged by centre regardless of the number of patients on each machine. To give a better indication of the variation in population dose with technique, the dose resulting from a particular technique was averaged over the total number of patients examined at the centres. These are included in Table V which gives the number of patients and the mean surface dose and score for each receptor type. All three film categories gave poor image scores with tungsten targets; with molybdenum, the highest score—though not the lowest dose—was obtained with the Du Pont Lo-Dose/Kodak MIN-R screen-film combinations, although all three film scores were close.

Medio-lateral view

All centres employed at least the two standard views. Although the surface dose from a medio-lateral view was not measured for every machine, exposure factors were noted which enabled the mean surface doses included in Table V to be assessed. The overall increases compared to the cranio-caudad views were 4% to 6% for xerox and 19% to 20% for film.

Maximum surface absorbed dose per examination

This may be as much as the sum of the surface doses for the individual views and is illustrated in Fig. 4. A nominal 10% has been added for repeat exposures.

TABLE IV

MEAN SURFACE ABSORBED DOSES AND IMAGE SCORES (PER CENTRE) FOR TARGET AND RECEPTOR COMBINATIONS FROM A SINGLE CRANIO-CAUDAD VIEW

Target–receptor	Mean surface dose (cGy (rad), ± s.d.)	Surface dose range (cGy (rad))	Mean image score (± s.d.)	Image score range
Molybdenum—film	1.19±0.98	0.09 to 3.40	33.0±3.7	25.6 to 39.2
Tungsten—film	0.59±0.30	0.33 to 1.25	24.7±5.2	17.6 to 34.6
Molybdenum—xerox	3.26±0.94	2.34 to 4.50	40.9±3.0	37.7 to 44.4
Tungsten—xerox	0.89±0.43	0.45 to 1.46	39.4±3.6	34.6 to 42.5

TABLE V

MEAN SURFACE ABSORBED DOSES AND IMAGE SCORES (PER CENTRE) AND MEAN SURFACE ABSORBED DOSES (PER PATIENT) FOR DIFFERENT TUBE TARGETS AND RECEPTORS, FROM A SINGLE CRANIO-CAUDAD (C-C) VIEW; ALSO ESTIMATED MEAN SURFACE DOSES (PER CENTRE) FROM A SINGLE MEDIO-LATERAL (M-L) VIEW

	Molybdenum target					Tungsten target				
Image receptor	No. of centres	Monthly no. of patients	Mean surface dose per centre and per patient (cGy (rad) c-c view)	Mean surface dose per centre (cGy(rad) m-l view)	Mean image score	No. of centres	Monthly no. of patients	Mean surface dose per centre and per patient (cGy (rad) c-c view)	Mean surface dose per centre (cGy (rad) m-l view)	Mean image score
Non-screen film	11	669	1.92 (1.51)	2.08	32.7	8	56	0.54 (0.48)	0.68	25.6
Fast-tungsten screen-film except Lo-Dose	5	1060	0.71 (0.20)	1.42	31.1	1	24	—	—	21.0
Lo-Dose/MIN-R screen-film combinations	25	1128	0.95 (0.87)	1.07	33.4	2	36	0.79 (0.94)	0.79	23.0
Film (overall)	41	2857	1.19 (0.83)	1.43	33.0	11	116	0.59 (0.61)	0.70	24.7
Xerox	7	984	3.26 (3.61)	3.39	40.9	8	752	0.89 (1.21)	0.94	39.4

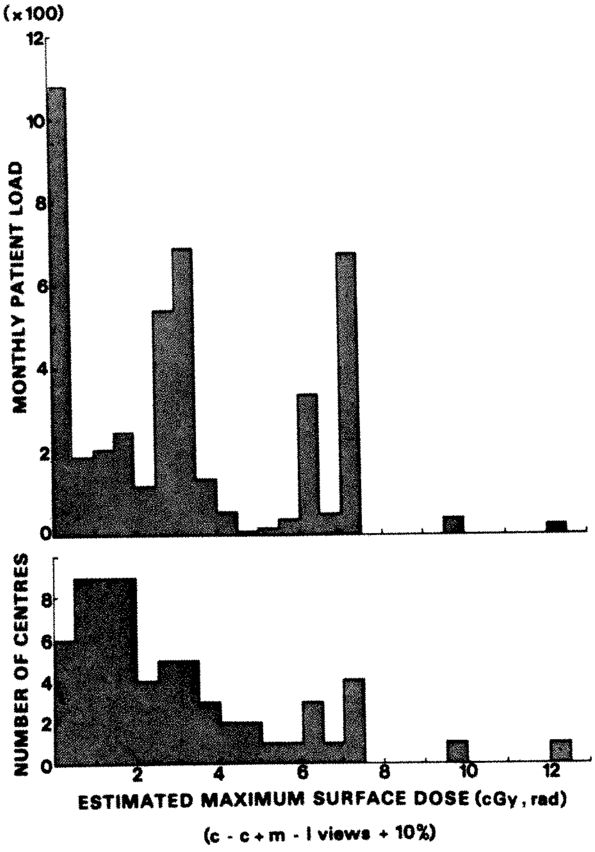


FIG. 4.

Histogram giving the monthly number of patients and the number of centres as a function of the estimated maximum surface dose from the examination of a single breast (cranio-caudad + medio-lateral + 10% for repeat exposures).

COMPARISON WITH PUBLISHED RESULTS

There are a variety of ways of expressing the quantity "radiation delivered to the patient", which makes direct comparison of results more difficult, as already noted by Boag *et al.* (1976), Bailar (1977) and Hammerstein *et al.* (1979). Boag *et al.* (1976) advocate the use of air kerma at the entrance plane for its lack of ambiguity and ease of conversion to other quantities. Absorbed dose per unit area for a given breast thickness is also suggested since it reflects the spatial distribution of dose with depth. Other quantities used are the "skin" dose, though this usually means the less ambiguous "surface" or "entrance" dose to a homogenous breast since the composition and depth of the basal cells of the epidermal layer are normally ignored (*e.g.* Evans *et al.*, 1975; Kindl *et al.*, 1978), mid-breast dose (Gilbertson *et al.*, 1970) and the mean tissue dose (Bailar, 1977); there seems to be no agreement as to which is the most useful form.

In addition, some authors have failed to specify how the absorbed doses were derived from measurements, or even how they were measured, to give calibration traceability and correction factors and to detail the assumed breast composition. Doses will be over-estimated by ~37% if water, rather than an average 50% fat/50% water composition, is used in the 20–50 keV region. Confusion has also arisen between dose per view and dose per examination.

Not surprisingly, other surveys have also shown a wide range of techniques and results. Bicehouse (1976) precipitated the continuing national surveys in the USA by reporting that 70 facilities in Pennsylvania gave surface air kermas for a single cranio-caudad view from 0.22 to 41 cGy (rad). The very high values often arose through over-exposure and under-development, especially if the high-density technique of mammography (Egan, 1960) was used. General X-ray units were used in 58 centres and only 12 had purpose-built sets. Mean values for the receptor types were generally higher than those reported here.

Jans (1977) in a pilot "Breast Exposure–Nationwide Trends" (BENT) survey of 238 facilities found that 24% used xerox to examine 40% of the total number of patients, giving surface doses between 0.22 and 6 cGy (rad) with a mean of 1.8 cGy for a cranio-caudad view. The effect of target material was not reported. Results for different receptors were similar to those from this survey.

Malone (1978) has reported on the progress made in the regular monitoring of the National Cancer Institute's Breast Cancer Demonstration Detection Projects by the Centres for Radiological Physics, which began in 1974. In the third year, 70% of the 47 systems visited were xerox (the reverse of the situation in Britain). A trend from molybdenum to tungsten targets using higher kilovoltages and aluminium filtration was recorded (from May 1976, Xerox 125 users in Britain and elsewhere were advised by the manufacturer to use additional aluminium filtration).

One result from the survey in New Zealand (Watson, 1977) was that the mean entrance dose using xerox was 68% greater than that for the Du Pont Lo-Dose system, both apparently with tungsten targets; from this survey, the doses were similar. Also, of the 18 centres included, only seven produced "good quality" (arbitrary scale) mammograms of a very simple phantom and 11/36 films taken were considered undiagnostic. Although not discussed, 14/15 of the film users appeared to employ a tungsten target tube which this paper and others have demonstrated to be unsatisfactory for film mammography.

The dose estimates quoted by various authors for individual centres and for different receptor types differ widely. The lowest surface dose recorded was 0.18 cGy (rad) to the upper inner quadrant (UIQ) for the *whole examination* (both breasts) by Asbury and Barker (1975) using the 3M Trimax rare-earth system, although no measure of "image quality" was given. This system was not in use at any centre visited during this survey, but surface doses for a cranio-caudad view of less than 0.2 cGy (rad) that gave close to the overall mean film score were noted at two centres.

Various estimates have been made of the "threshold" values of the smallest detectable sizes of calcifications. Using breast sections containing actual calcifications, Millis *et al.* (1976) found thresholds of ~0.1 mm for xerox and ~0.4 mm for film (screen and non-screen), and Tonge *et al.* (1976) observed that the threshold was dependent on the type of film. They identified the 0.1 to 0.3 mm size range as being clinically important and found only Kodak Crystallex film to be superior to xerox overall (molybdenum and tungsten targets), but xerox to be better below 0.2 mm. Evans *et al.* (1975) found that with a molybdenum target the thresholds were ~0.1 mm for xerox and ~0.15 mm for film.

A homogeneous phantom, such as was used for this survey, produces unrealistically low image noise which may lead to enhanced thresholds, and should be used for ranking only. Bearing this limitation in mind, the results presented here suggest that with the phantom employed, for calcification (silicon) cubes the threshold was generally 0.20 to 0.25 mm for xerox and 0.30 to 0.35 mm for film (overall), whereas for filaments, there was a lower threshold due to their long axial dimension.

CONCLUSIONS

1. A diversity of mammographic techniques is currently practised in Britain and no combination has been highlighted as being superior in terms of both dose and image score—only a controlled comparison of the techniques available would elicit the best combination. The commonest systems (by May 1978) were the molybdenum target/Du Pont Lo-Dose or Kodak MIN-R screen-film combinations (48%) and molybdenum or tungsten target/xerox (13% each).

2. The limitation of the phantom, *i.e.*, the fixed geometry of the test objects, must be borne in mind when the results presented here are examined. Every effort was made to include realistic details in the phantom, and it appears to be a sufficiently sensitive yardstick of "image quality as measured by a phantom" in that a range of scores resulted (from 22% to 60% of the maximum obtainable.)

3. The most important results relate to the choice of target and receptor type. In order of *decreasing* surface dose, they were: molybdenum/xerox > molybdenum/film > tungsten/xerox > tungsten/film. In order of *increasing* "image quality score" they were: tungsten/film < molybdenum/film < tungsten/xerox < molybdenum/xerox.

The technique of choice for asymptomatic screening appears to be molybdenum/film or tungsten/xerox. The results for the molybdenum/xerox combination seem to justify its use for symptomatic diagnosis only and it is suggested that the use of the tungsten/film combination is abandoned. It is clear that a majority of patients (over 60%) were possibly receiving absorbed doses to the breast surface exceeding the 2 cGy (rad) limit per examination suggested by Ellis (1972) as acceptable in population screening.

4. As already noted, there is a spectrum of mammographic methods and results with some centres producing very poor quality images. If widespread screening programmes are to be established in Britain, further work is required to establish the optimum technique(s) and to have these adopted and maintained nationally. Only then can a common high standard be achieved. Some standardization of X-ray equipment, agreement on the specification of the radiation delivered to the patient and the implementation of quality assurance have been suggested as useful goals in the USA (Bicehouse, 1978). Similar moves in Britain are desirable.

ACKNOWLEDGMENTS

We would like to acknowledge the co-operation of the radiologists and radiographers in the 61 centres included in this survey. We thank Dr. W. E. Liversage, Dr. A. K. Tucker, Dr. J. Law and members of the Diagnostic Radiology Topic Group of the Hospital Physicists' Association (1977–1978) for helpful discussion. We also thank manufacturers of X-ray equipment and receptors for helpful comments. Thanks are also due to Mr. H. Venner, Mr. A. Rickwood and Mr. R. Darlison for the construction of equipment, Mr. M. A. Bullen for the design and manufacture of the electrometer test device, Mr. B. E. Keane for assistance with the ionization chamber calibrations and loan of an ^{241}Am photon source, Dr. D. W. Miller (Memorial Sloan-Kettering Cancer Centre, New York) for calibrating some of the TL chips for comparison purposes, Dr. C. Constantinou and Mr. D. Mayes for scoring the films and xeromammograms, Mr. A. W. Dunlop for the curve-fitting and Mrs. J. Wadsworth for statistical analyses.

REFERENCES

ASBURY, D. L., and BARKER, P. G., 1975. Radiation dosage to the breast in well-women screening surveys. *British Journal of Radiology*, *48*, 963–967.

BAILAR, J. C., 1976. Mammography: a contrary view. *Annals of Internal Medicine*, *84*, 77–84.

BAILAR, J. C., 1977. Screening for early breast cancer: pros and cons. *Cancer*, *39*, 2783–2795.

BICEHOUSE, H. J., 1976. Survey of mammographic exposure levels and techniques used in Eastern Pennsylvania. In *Assuring Radiation Protection.* 7th Annual National Conference on Radiation Control, pp. 136–143. FDA 76-8026. (Bureau of Radiological Health, Maryland, USA).

1978. Mammography (Task Force No. 15). In *Meeting Today's Challenges.* 9th Annual National Conference on Radiation Control, pp. 185–187. FDA 78-8054 (Bureau of Radiological Health, Maryland, USA).

BOAG, J. W., STACEY, A. J., and DAVIS, R., 1976. Radiation exposure to the patient in xeroradiography. *British Journal of Radiology*, *49*, 253–261.

BRITISH JOURNAL OF RADIOLOGY, 1972. *Supplement No. 11. Central Axis Depth Dose Data for Use in Radiotherapy.* Ed. M. Cohen, D. E. A. Jones and D. Greene (British Institute of Radiology, London).

EGAN, R. L., 1960. Experience with mammography in a tumour institution: evaluation of 1000 studies. *Radiology*, *75*, 844–900.

ELLIS, R. E., 1972. Breast cancer following irradiation. *British Journal of Radiology*, *45*, 795–796.

EVANS, A. L., JAMES, W. B., MCLELLAN, J., and DAVISON, M., 1975. Film and xeroradiographic images in mammography. A comparison of tungsten and molybdenum anode materials. *British Journal of Radiology*, *48*, 968–972.

GILBERTSON, J. D., RANDALL, M. G. ,and FINGERHUT, A. G., 1970. Evaluation of roentgen exposure in mammography. Part II: Four views. *Radiology*, *97*, 641–647.

HAMMERSTEIN, G. R., MILLER, D. W., WHITE, D. R., MASTERSON, M. E., WOODARD, H. Q., and LAUGHLIN, J. S., 1979. Radiation absorbed dose in mammography. *Radiology*, *130*, 485–491.

HOSPITAL PHYSICISTS' ASSOCIATION (HPA), 1976. *The Physics of Radiodiagnosis.* Scientific Report Series No. 6 (Hospital Physicists' Association, London).

JANS, R. G., 1977. The options: mammography quality assurance program. In *Radiation benefits and risks: Facts, issues and options.* 8th Annual National Conference on Radiation Control. pp. 233–239. FDA 77-8021 (Bureau of Radiological Health, Maryland, U.S.A.).

KINDL, P., SPREIZER, H., and SCHNEIDER, G., 1978. Dosimetry in examinations carried out with the Mammomat. *Electromedica*, *46* (*1/78*), 28–31.

MALONE, W. F., 1978. National Cancer Institute's guidelines for mammography. In *Meeting Today's Challenges.* 9th Annual National Conference on Radiation Control, pp. 51–59. FDA 78-8054 (Bureau of Radiological Health, Maryland, U.S.A.).

MILLIS, R. R., DAVIS, R., and STACEY, A. J., 1976. The detection and significance of calcifications in the breast: a radiological and pathological study. *British Journal of Radiology*, *49*, 12–26.

RUDEN, B. I., 1976. Evaluation of the clinical use of TLD. *Acta Radiologica Therapy Physics Biology*, *15*, 447–464.

TONGE, K. A., DAVIS, R., and MILLIS, R. R., 1976. The problem of discrimination in mammography. Arguments for using a biological test object. *British Journal of Radiology*, *49*, 678–685.

WATSON, P., 1977. A survey of radiation doses to patients in mammography. *British Journal of Radiology*, *50*, 745–750.

WHITE, D. R., and TUCKER, A. K., 1980. A test object for assessing image quality in mammography. *British Journal of Radiology*, *53*, 331–335.

WHITE, D. R., MARTIN, R. J., and DARLISON, R., 1977. Epoxy resin based tissue substitutes. *British Journal of Radiology*, *50*, 814–821.

Book reviews

Die Röntgenuntersuchung im Kindesalter (*X-ray Procedures in Childhood—Techniques and Indications*). By K. D. Ebel and E. Willich. 2nd ed., pp.viii+308, 1979 (Springer Verlag, Berlin). DM88 $48.40.
ISBN 3-540-08969-1

The second edition of this German book is again written for both radiologist and radiographer. While some examinations have been excluded, new techniques have been added, including scintigraphy, cavography, ultrasound and CT. The angiography section has been enlarged. Descriptions of these procedures make the book of more interest to the radiologist than the previous edition. Though various tips concerning the difference of approach between paediatric and adult patients are useful, it seems to the reviewer that some of the descriptions of basic techniques are superfluous.

The alphabetical index of diagnoses and indications for appropriate examinations has been enlarged and is once again one of the very useful sections of this book, both for the radiologist and for the radiographer inexperienced in paediatrics.

Like the first edition, this book would be a useful addition to any X-ray department if it were in English.

A. WULACH.

A Professional Approach to Radiology Administration. By R. R. Osborn. pp. xiii+213, 1980. (Charles C. Thomas, Springfield, Illinois). $29.75.
ISBN 0-398-04097-4

This book, by royce r. osborn [*sic*], Assistant to Diagnostic Division Chief, Department of Radiological Science UCLA School of Medicine, Los Angeles, with 30 years' experience in the field of radiology, "delineates the role of the professional radiology administrator". Much, if not most, of this book is irrelevant to administrators in radiology (and other) departments in the National Health Service, and what little there is is very basic. Aspiring administrators of X-ray departments in the NHS would gain more from talking to Hospital Secretaries than from reading this book.

T. HEALES.

1981, *British Journal of Radiology*, 54, 221–231 MARCH 1981

Evaluating performance characteristics in computerized tomography

By *D. R. White, Ph.D., †R. D. Speller, Ph.D. and *P. M. Taylor, B.A.

*Radiation Physics Department, St. Bartholomew's Hospital, London EC1A 7BE and
†Department of Physics as Applied to Medicine, Middlesex Hospital Medical School, London W1P 6DB

(Received November 1979 and in revised form August 1980)

ABSTRACT

The important radiographic and dosimetric performance parameters associated with computerized tomography (CT) are discussed together with the practical problems encountered when they are being evaluated. The parameters include alignment, slice thickness, noise, low-contrast detectability, spatial resolution, modulation transfer function and patient dose. A set of phantoms for determining these performance characteristics are described. The phantoms are of modular construction permitting measurement of the performance parameters at various sites within a number of 6 cm thick, regular-geometry, and realistic body sections. The regular-geometry sections include 20 cm diameter (skull size) and 33 cm diameter (abdomen size) sections. The realistic anthropomorphic sections include the skull, abdomen and thorax.

In recent years the number of CT systems in clinical use has greatly increased with ever-increasing improvements in performance. Fortunately, following the pioneering work of McCullough and his associates, the physical parameters requiring evaluation are well documented in the literature (McCullough *et al.*, 1974; 1976; AAPM, 1977). Problems arise when the important parameters are being measured to the accuracy necessary with the current generation of high sensitivity CT machines. Experience has shown (Speller *et al.*, 1981a; b) that very careful measurements with elaborate test objects are essential, and that simple water-filled phantoms and many of the so-called "customer phantoms" supplied by manufacturers have limited applications.

In this communication, the important performance parameters requiring evaluation are outlined and problems in their derivation are discussed. A range of phantoms developed for use with all models of CT machines currently in production are described. As well as attempting to establish precisely the performance characteristics, the realistic phantoms will be shown to provide data directly applicable to the clinical situation.

PARAMETERS REQUIRING EVALUATION

At least nine categories of performance parameters should be considered in any evaluation of a CT system. After the mechanical alignment of the system has been shown to be acceptable and the slice thickness established, the important parameters relating to noise, uniformity of CT numbers, low contrast detectability, spatial resolution, modulation transfer function and dose to the patient have to be evaluated. Finally, effective energy and linearity of CT numbers should be investigated. Although these parameters are not strictly independent of each other, for convenience they will be outlined separately in this section.

Alignment

Mechanical alignment of the CT machine may be readily checked by scanning a phantom containing a small, high-contrast object such as an air hole or aluminium rod (McCullough *et al.*, 1976) positioned perpendicular to the image plane. Misalignment produces streaking artefacts in the reconstructed image.

Slice thickness

Rows of equally-spaced high-contrast beads or wires inclined at a known angle to the image plane may be used for approximate determinations of slice thickness in scans of high spatial resolution (Goodenough *et al.*, 1975). The method of choice for more precise work is the use of aluminium plates inclined generally at 45° to the plane of the X-ray beam (AAPM, 1977) or at smaller angles for narrow slices ($\leqslant 5$ mm), when the slice thickness may be derived from the full-width-half-maximum (FWHM) obtained from a profile of averaged CT numbers. Accurate results can only be achieved if the angle of inclination is known precisely. For example, errors of 5 or 10° due to the bad orientation of a phantom containing a 45° aluminium plate can cause errors in a 10 mm slice thickness of 2 and 4 mm respectively.

Orientation errors may be evaluated by using two aluminium plates inclined at different angles. When scanned together and the resulting profiles of CT number plotted, any orientation error, which applies to both aluminium plates, may be assessed and the corrected values for slice thickness calculated. In practice this technique is only successful if the two profiles of CT number can be accurately established, as uncertainties can give spurious orientation errors resulting in discrepancies in the derived slice thickness.

Another method of evaluating orientation errors is again to use dual aluminium plates, but this time having nominally the same angle (ϕ) on either side of the X-ray beam axis, that is, in the form of an "X" (Fig. 1). Any orientation error (θ) will be positive for one plate and negative for the other and can readily be evaluated from the equations $s=x_1 \tan(\phi+\theta)$ and $s=x_2\tan(\phi-\theta)$, where s is the slice thickness and x_1, x_2 the FWHM values obtained from the two profiles of CT number. When the angle ϕ is made equal to 45°, the equations resolve into the useful relationship, $s^2=x_1 x_2$.

Noise

This parameter is defined conventionally as the standard deviation (σ) of the mean CT number obtained on scanning a region of interest within a homogeneous phantom (McCullough *et al.*, 1974; 1976). If different scanners are being compared, the value of σ may be expressed as a percentage of the difference between the CT numbers for water (H_w) and air (H_a), or

$$100\sigma/(H_w-H_a)\ \%.$$

For reliable determination of noise, the phantom must have a high degree of homogeneity. Trapped air in water phantoms and the use of badly mixed polymers or resins containing particulate fillers must be avoided.

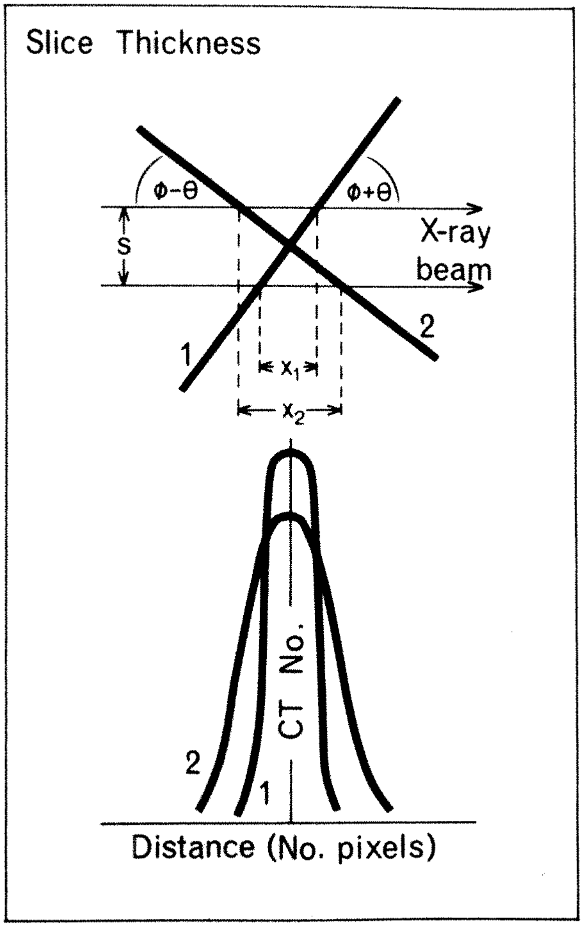


FIG. 1.

The determination of slice thickness using a pair of inclined aluminium plates, nominally at angle ϕ to the X-ray beam axis, with an orientation error θ.

Uniformity of CT numbers

The spatial uniformity of CT numbers may be evaluated by comparing the mean values at central (H_1) and peripheral (H_2) locations within a large, uniform phantom (*e.g.* water-filled Perspex container). For intercomparisons of different scanners, the maximum variation of H_1 and H_2 may be obtained and expressed as a percentage of the difference between the CT numbers for water and air,

$$100(H_1-H_2)/(H_w-H_a)\ \%.$$

This method has been adopted in preference to the possibly more tedious technique of comparing profiles of CT number across the phantom and determining the fraction of the profile that lies within $\pm 2\sigma$ of the modal number (HPA, 1980).

Care must be taken to position the phantom centrally in the scan field, and the phantom must have a high degree of homogeneity.

Low-contrast detectability

By scanning small, low-contrast objects contained in a suitable phantom, detectability may be assessed subjectively as the minimum size detectable (AAPM, 1977). Rods or beads of polystyrene, a few millimetres in diameter, are acceptable in water or solid water-substitute phantoms. These would give a 3% contrast (*i.e.*, $\mu_{\text{polystyrene}}/\mu_{\text{water}}=0.97$ at 70 keV). Problems with water phantoms may arise due to air bubbles forming around the immersed polystyrene, highlighting otherwise unobservable objects. Beads can only be employed if embedded in phantoms based on solid polymer or resin. Caution is required in the comparison of sensitivity from machines operated at different kilovoltages, as the contrast of polystyrene compared to water varies from 5% to 2% as the effective photon energy changes from 60 to 80 keV.

Spatial resolution

This parameter may be established subjectively by scanning arrays of small rods or beads (McCullough, 1976) composed of a high-contrast material (*e.g.* cortical bone substitutes, Perspex, etc.) and arranged in rows in a water or water-like phantom. Rows containing five rods or beads spaced at a distance equal to the diameter are scanned and the diameter of the smallest set imaged as five discrete items is a measure of the resolution. As with detectability, the problem of air bubbles forming around the objects must be considered in water-filled phantoms.

Another interesting problem with measurements of both detectability and resolution is the presence of orientation errors, which are illustrated in Fig. 2. An X-ray beam with a slice thickness (s) of 10 mm is used to scan a low-contrast rod (*e.g.* 3 % contrast) of 1 mm diameter. Pixel size (p) is assumed to be 1 mm. If the orientation is ideal (Fig. 2a), the rod is parallel to the pixel arrays and is reconstructed according to the CT number profile shown in Fig. 2c, and the display will depict a small low-contrast area. An indication of the magnitude of the noise (σ) present in a typical scan is given in the figure, together with a $\pm 2\sigma$ variation associated with individual pixels. If the orientation is not correct, the situation shown in Fig. 2b could exist where the visibility of the low-contrast object deteriorates until, at an orientation error (θ) of $\tan^{-1}(s/p) = 5.7°$, the rod cannot be positively identified because of the noise of the system. This reduction in detectability is totally due to bad orientation and not to any performance anomaly with the machine. Similar problems occur with arrays of high contrast rods used in resolution patterns when orientation errors could cause the resolution apparently to deteriorate. For both detectability and resolution, this effect is more important as the contrast of the objects decreases and the noise of the system increases.

False results can also occur with test pieces using beads, if they are inaccurately positioned within the X-ray slice. For reliable data, beads must always be positioned in the central, high-sensitivity region of the slice.

Modulation transfer function

Estimates of spatial resolution made with rod patterns suffer from their dependence upon the observer's assessment of the image. A more quantitative approach for measuring spatial resolution is to consider the modulation transfer function (MTF). Traditionally, the MTF has been derived as the Fourier transform of the point spread function (PSF) —the response of the system to an impulse (Rossman, 1971). For many applications outside the field of CT this approach does not compromise the result, but direct measurement of the PSF in a CT scanner (*e.g.* the image of a thin, high-contrast wire) leads to very few data points that can define the PSF (Bischof and Ehrhardt, 1977; McCullough *et al.*, 1976). Averaging several images will cause the MTF to be degraded by increasing the effective width of the PSF. The contours of CT number in Figs. 3a and 3b demonstrate the difficulty of obtaining a unique function for the PSF. A 2 mm diameter Perspex rod (Fig. 3a) presents the problem that its size is such that it can no longer be considered as an impulse. The resulting MTF (curve 1, Fig. 3e) shows structure that is generated by the relatively low signal to noise ratio and the fact that the "impulse" diameter represents several pixels. The use of impulse response functions to represent the PSF can be improved by application of the CT number contour plots. Careful selection of the impulse material and rotation of the contour enables the most suitable PSF to be selected and spurious data points to be avoided. For example, the 0.27 mm NiCr wire impulse (Fig. 3b) leads to an adequate representation of the MTF.

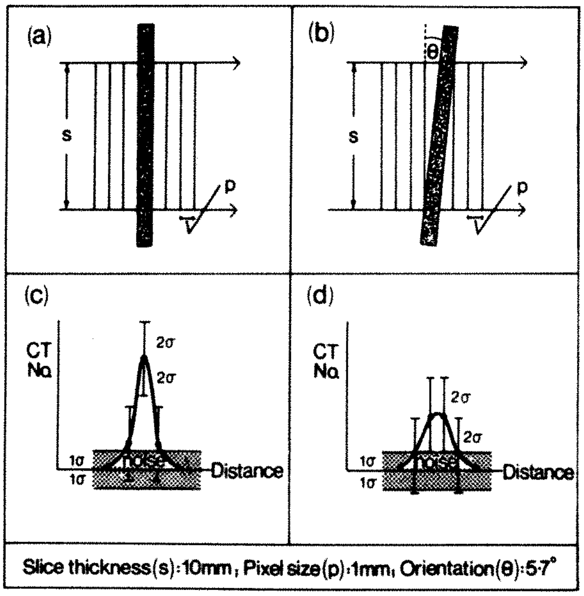


FIG. 2.

The effect of orientation errors on the evaluation of low contrast detectability.

As an alternative approach to avoid the problems associated with point responses, Judy (1976) has suggested the use of an interface to give the edge response function (ERF), the first derivative of which gives the line spread function (LSF), which

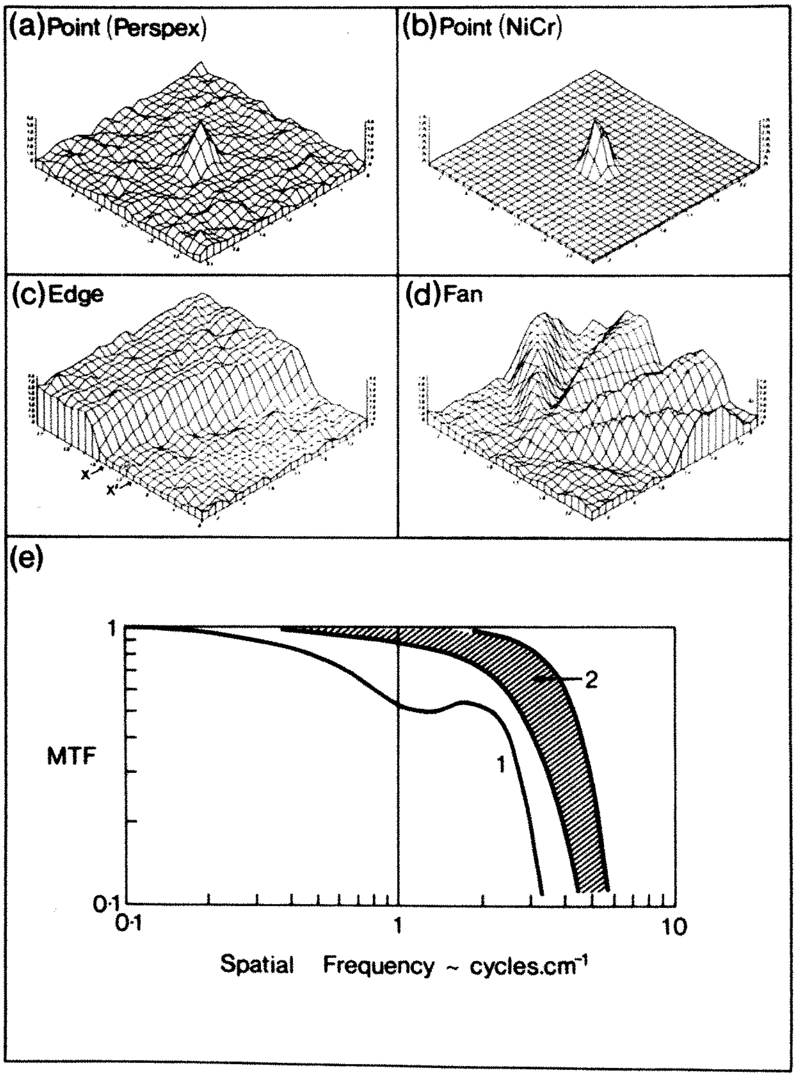


FIG. 3.

Typical contours of CT number for (a) point (Perspex); (b) point (NiCr); (c) edge; (d) fan and (e) the resulting MTF curves measured on a CT5005 scanner operating in the brain mode with a "slow" scan and reconstruction over a 320 × 320 matrix.

in an isotropic system can be considered as the PSF. Accurate values of ERF can be generated by inclining the interface (*e.g.*, Perspex–water) so that it maintains a small angle (2–8°) to the rows or columns of the image matrix. In this way the number of data points defining the ERF is increased. Plots of any of the pixel lines between x and x' of Fig. 3c can be used as a representation of the ERF as shown in Fig. 4a.

Correction of the data spacing along the ERF is performed using the relationship:

Effective pixel size = true pixel size. sin ϕ

thus giving a ten to 25 fold increase in data points per ERF for $\phi = 8$ to 2° respectively.

The materials chosen for the interface must be selected to give a large signal to noise ratio without the size of the edge in the image plane causing artefacts. Perspex in water or water substitute material represents a suitable choice.

A direct method for calculating the MTF has been demonstrated by MacIntyre *et al.* (1976). They have estimated the modulation in the image of a fan test pattern by direct inspection of the CT number print-out. The spatial frequency at which the measured modulation occurs is derived from the dimensions of the wedges and the distance between the measurement point and the apex of the fan (Fig. 4b). A typical response to such a pattern is shown in Fig. 3d. This method gives results that suffer from poor statistical meaning at higher spatial frequencies since the size of the fan pattern becomes comparable to the pixel size at these frequencies with an associated increase in noise.

MTF curves derived from NiCr point, Perspex edge and Perspex fan responses are generally in close agreement, falling within the shaded area shown in Fig. 3e (area 2).

Dose received by the patient

Although the most appropriate method of interpreting the risk to the patient due to the radiation from a CT scan is still being debated, it is imperative that a measure of the radiation dose should be established. Ionization, photographic film and TL dosimetry have been reported in the literature (Jucius and Kambic, 1977). A combination of film to identify any peak doses, together with arrays of TLD ribbons or chips positioned across the slice and irradiated on edge using a suitable phantom appears to be a good compromise. It is better to evaluate doses in a single slice so as to avoid anomalous results due to inaccurate couch movements when using multiple slices. Once the dose profile from a single slice has been estimated, multiple slice data can be readily calculated. Errors in orientation and positioning of the phantom are often the cause of inconsistent results.

Effective energy and linearity of CT numbers

The techniques introduced by White and Speller (1980) for establishing both an effective energy (E_{eff}) and the linearity of the relationship between linear attenuation coefficient (μ) and CT number, have been extensively tested on over 50 CT scanners and found to be very reliable. Basically, samples of specially prepared liquid mixtures (KeVliquids) having the same μ-values as water at specific energies, are scanned in a suitable phantom, together

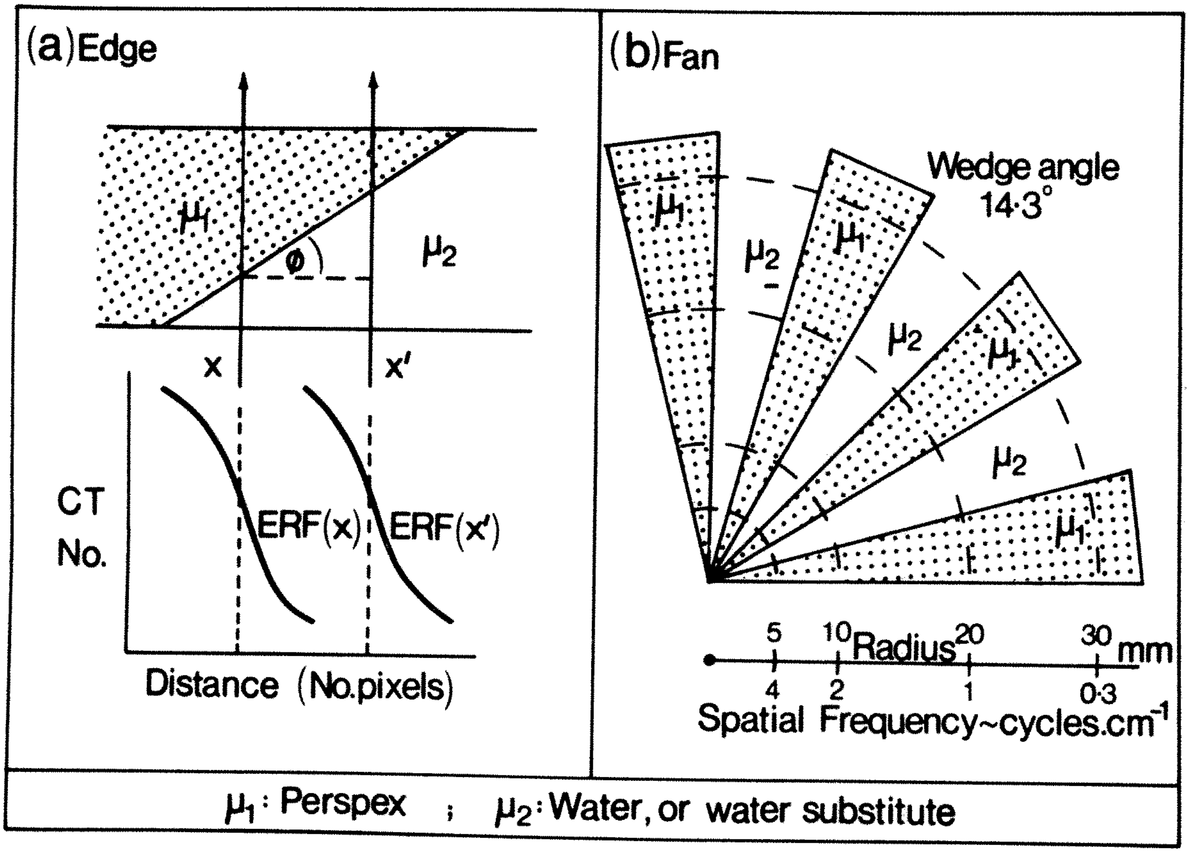


FIG. 4.
Schematic representation of the derivation of MTF using (a) edge and (b) fan responses.

with a water sample. The mixture with the same CT number as water is indicative of an effective X-ray energy at the measurement site. Knowing this energy, the μ-values of the individual KeVliquids are calculated so that a relationship of the form:

$$\mu = a_1(\text{CT number}) + a_0,$$

where a_1, a_0 are constants, may be fitted by the method of least squares to the corresponding values of μ and CT number. For accurate results, high purity liquids and de-gassed water must be used and corrections made for variations in temperature.

MATERIALS AND METHOD

The design and manufacture of the performance phantoms developed in this study were based on four basic requirements.

(i) The design should permit all of the important performance parameters to be measured with the requisite accuracy, at different locations within regular-geometry and anthropomorphic sections. This would enable performance variations to be evaluated across the reconstruction area in idealized and realistic situations.

(ii) The phantoms should be simple to use and capable of being rapidly prepared—an important consideration with the present high work-loads of CT machines.

(iii) If possible, the design should allow future evaluation techniques to be readily included without major modifications to the phantoms.

(iv) The phantoms should be appropriate for all types of CT scanners currently in production so that comparative surveys could be undertaken.

The basic requirements appeared to point to solid phantoms having a modular construction and resulted in manufacture of the set of phantoms shown in Fig. 5. Epoxy-resin-based substitute materials (White *et al.*, 1977) were employed extensively and allowed evaluation test pieces to be embedded in conical plugs ("evaluation inserts") 7 cm high, 4.5 cm diameter at the centre of the scan slice and with a 10° non-locking taper. Homogeneity and reproducibility of the substitute materials were controlled by the use of fine particulate fillers and vacuum-mixing and vacuum-pouring techniques (White and Constantinou, 1981), with batch-to-batch variations in μ-values of the water substitute used being about 0.5%. The water substitute, together with the low contrast materials suitable for liver, kidney and heart, was produced by simply varying the filler concentration of the muscle substitute MS11 (White *et al.*, 1977) and gave good simulation for photon interaction over the energy interval 60–90 keV. Metal moulds were used for casting the plug inserts and the cavities in the sections which accepted the inserts.

The photographs in Fig. 5 show that eight types of regular geometry and anthropomorphic sections were manufactured, the latter being based on the body sections of Symington (1917), Eychleshymer and Shoemaker (1970) and Gambarelli *et al.* (1977). The sections, all 6 cm thick and containing from one to nine cavities, are outlined below:

(i) 20 cm diameter water substitute with five cavities and 4 mm cortical bone substitute ring (Fig. 5a);

(ii) 33 cm diameter water substitute with nine cavities (Fig. 5b);

(iii) anthropomorphic skull (including orbits), composed of four tissue substitutes, with two cavities (Fig. 5a);

(iv) anthropomorphic skull (including orbits and petrous bones), composed of four tissue substitutes, with one cavity (Fig. 5a);

(v) anthropomorphic skull cap, composed of two tissue substitutes, with one cavity and surface channels for TLD holders (Fig. 5d).

(vi) anthropomorphic upper abdomen, composed of nine tissue substitutes (including liver, kidney and contrast media/air interface), with one cavity (Fig. 5c);

(vii) anthropomorphic mid-thorax, composed of eight tissue substitutes (including lungs and heart), with three cavities (Fig. 5c);

(viii) as (vii) but with one cavity and with surface channels for TLD holders (Fig. 5d).

In order to reduce significantly the quantity of air trapped around the conical plug inserts when they are fitted into these sections, a water substitute was used in the form of a thixotropic gel, based upon the synthetic gelling agent Laponite XLG (Laporte Industries Ltd). The gel, designated "BL8", comprises water (70.36); glycerol (3.15); ethanol (22.00); Laponite XLG (4.49) (in percentages by weight), and has a mass density of 1000 kg m^{-3}. The elemental composition of BL8 is H (11.10); Li (0.02); C (12.71); O (74.16); Na (0.10); Mg (0.69); Al (0.004); Si (1.22); Ca (0.002); Fe (0.001) (in percentages by weight). The μ-data for BL8 are within 1% of similar data for water over the energy interval 60–90 keV.

A set of 75 performance inserts is now available. In addition to evaluation test pieces which are all embedded in a water substitute, homogeneous plugs of water, brain, muscle, lung and heart substitute are included. These allow the regular-geometry sections to be made uniform and the anthropomorphic

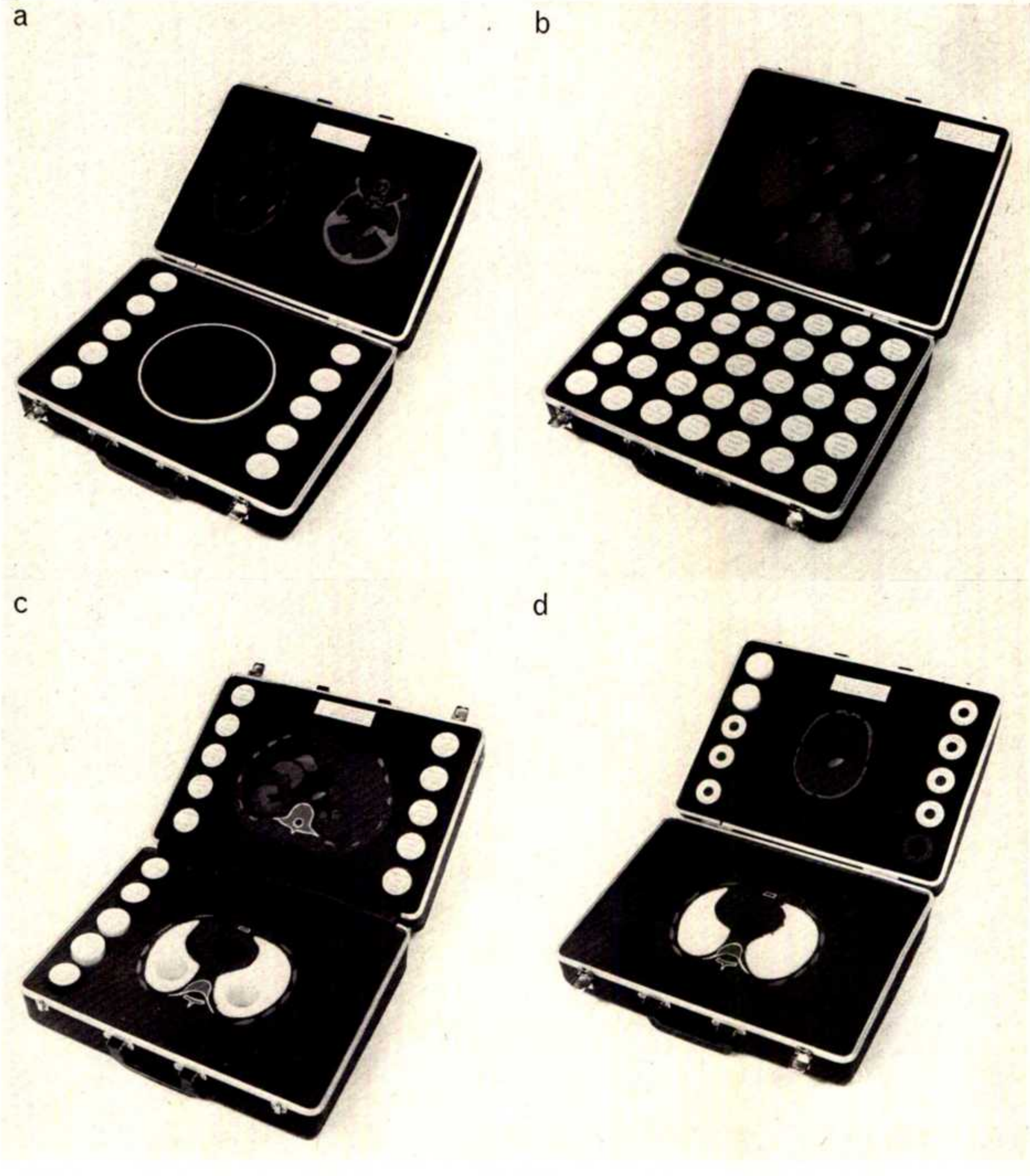


FIG. 5.

Photographs of CT evaluation phantoms. (a) Anthropomorphic and 20 cm diameter regular-geometry skulls. (b) Range of performance inserts and 33 cm diameter regular-geometry body. (c) Abdomen and thorax phantoms. (d) Skull and thorax phantoms for dosimetry.

sections to be completed. Inserts for ionization chambers and TLD holders are also available for the specialized dosimetry phantoms (Fig. 5d), together with plugs with central holes (Fig. 5c) to accommodate tubes of liquids.

The principal categories of evaluation inserts are

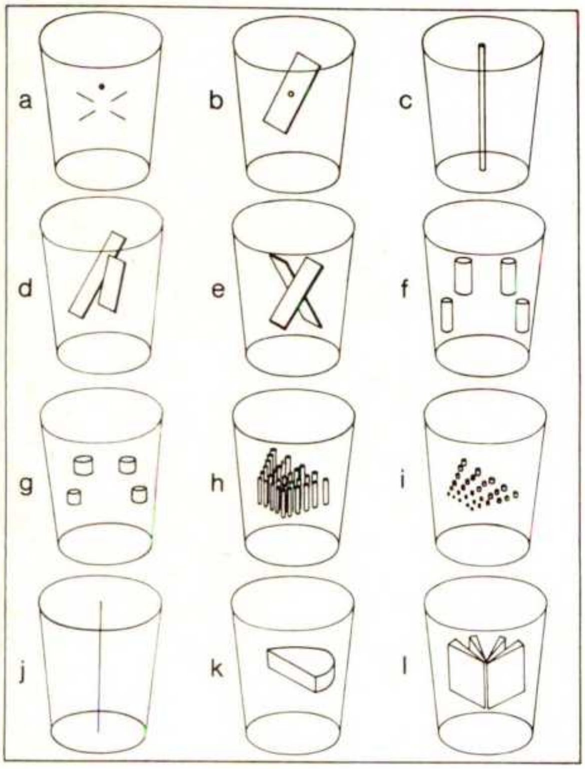


FIG. 6.

Schematic diagram illustrating the different types of evaluation inserts. (a) Cross-wires and bead (Pb) (orientation). (b) Inclined (45°) Al plate (0.72 mm thick) with central hole (position). (c) Al rod (3.17 mm dia) (alignment). (d) Dual angle (30°/45°) inclined Al plates (0.72 mm thick) (slice thickness). (e) X-inclined (45°) Al plates (0.72 mm thick) (slice thickness, orientation, position). (f) Polystyrene rods (1–15 mm dia., 1 mm steps) (detectability). (g) Polystyrene beads (1–15 mm dia., 1 mm steps—equal dia/height) (detectability). (h) SB3/Perspex rods (0.5–2.5 mm dia., 0.25 mm steps) (resolution). (i) SB3/Perspex beads (1–15 mm dia., 1 mm steps: equal dia/height) (resolution). (j) NiCr wire (0.27 mm dia) (MTF). (k) Perspex edge (MTF). (l) Perspex fan (MTF).

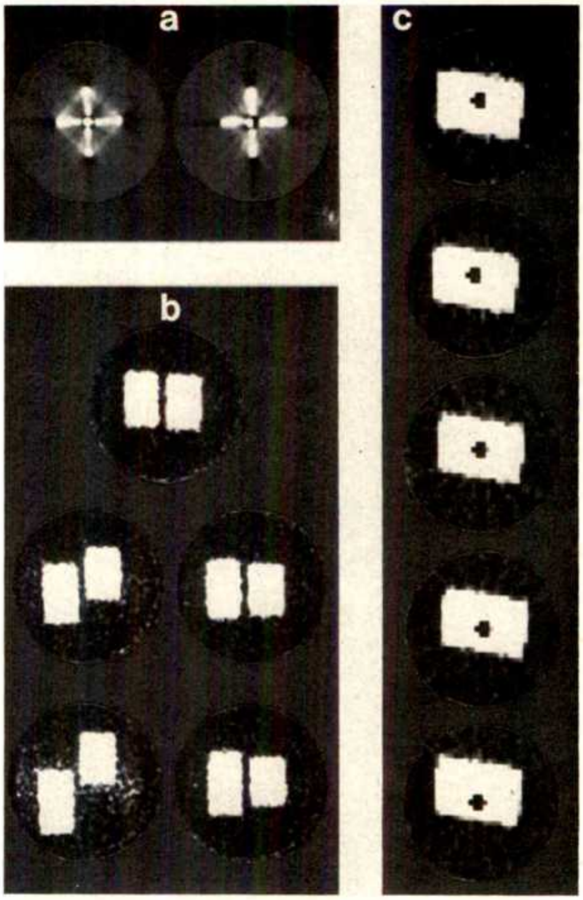


FIG. 7.

Examples of CT scans for checks of orientation and position (a) Cross-wires and bead insert; left: good orientation; right: 5° orientation error. (b) Pair of inclined plates; top: good orientation; middle left: 3 mm position and 2° orientation errors; middle right: 2° orientation error only; bottom left: 7 mm position and 4° orientation errors; bottom right: 4° orientation error only. (c) 45° inclined plate with central hole, 1 mm positional increments.

shown schematically in Fig. 6. Special attention has been given to the problem of orientating and positioning the phantoms correctly. A test piece for specifically recording errors of orientation is shown in Fig. 6a. Cross-wires of 1 mm diameter lead solder, with a central 3 mm gap, are set in a plane 8 mm from a 0.5–1 mm diameter lead bead. When scanned under ideal conditions, the bead appears at the centre of the cross-wires (Fig. 7a). As the orientation error increases from 1 to 7°, the image of the bead will first elongate and then be displaced from the central position. Horizontal and vertical orientation errors can be recorded. An even more sensitive indication of orientation errors has been noted with the slice thickness test piece using a pair of aluminium plates 0.72 mm thick inclined at 45° (Figs. 6e and 7b). Orientation errors as low as 2° are evident when the images of the two aluminium plates are of unequal length. Displacement of the two images about a central point indicates that a positional error is present (that is, the centre of the X-ray slice is not at the centre of the phantom test pieces) (Fig. 7b).

An insert designed specially for checks of position is shown in Fig. 6b, which comprises a 45° inclined aluminium plate (0.72 mm thick) with a central 2 mm hole. Positional changes of 1 mm are easily imaged as the light, high attenuation image of the aluminium plate tracks across the black spot image of the air hole (Fig. 7c).

Once the selected section is correctly orientated and positioned, all of the important parameters may be measured.

Alignment may be assessed using the aluminium rod insert (Fig. 6c).

Slice thickness is measured by either the dual angle (Fig. 6d) or the pair of aluminium plates inclined at 45° (Fig. 6e). The latter method is preferred, resulting in determinations of slice thickness with expected errors of less than 0.5 mm.

Noise may be evaluated at selected sites using any of the regular-geometry sections fitted with plain plugs of water substitute. Alternatively, by use of the inserts with the central hole shown in Fig. 5c, tubes (preferably with an added vertical section to eliminate problems with trapped air in the scanned region) filled with water may be used. Minor edge effects around the plug–cavity interface, due to a combination of the residual, minute volumes of trapped air and the pure resin shell produced around cast epoxy resin substitutes, mean that measurements should generally be restricted to areas away from the edges of plugs.

Uniformity of CT numbers may be assessed in a similar fashion to noise, using either plain plugs or tubes of water.

Low-contrast detectability is measured with either rod or bead test pieces (Figs. 6f and 6g) with an expected error of ±0.5 mm.

Spatial resolution is similarly measured with either rod or bead test patterns (Figs. 6h and 6i) with an expected error of ±0.13 mm.

Modulation transfer function in terms of point, edge and fan responses (Figs. 6j, 6k, 6l) are feasible. The accuracy of the MTF determination is probably better than 0.2 cycle cm^{-1} at the 50% cut-off.

Dose to the patient may be assessed for either single or multiple slices at the surface and centre of the special skull and thorax sections using film or TL dosimeters. To establish full side-scatter in use, the dosimetry sections are sandwiched between a pair of 5 cm thick slabs of Plexiglas shaped to the external contours of the sections. The total overall uncertainty in the measured dose should not exceed 10%.

Effective energy and linearity of CT numbers are investigated using the specially prepared KeV liquids (White and Speller, 1980), and are generally evaluated at the centre of the 20 and 33 cm diameter regular-geometry phantoms completed with plain plugs of water substitute. The liquids are contained in polypropylene tubes fitted into the sections with the aid of the inserts with the central hole. Uncertainties in published attenuation data result in a maximum error in the effective energy of about 3 keV and in linearity slopes, a_1, with expected errors of less than 5%.

From an inspection of Fig. 5, it will be evident that, with the exception of dose to the patient, each of these evaluation parameters may be determined at any of the 21 sites contained within six regular geometry and anthropomorphic skull and body sections.

A selection of typical CT scans from both regular geometry and anthropomorphic phantoms are shown in Fig. 8. Performance inserts for low-contrast detectability, spatial resolution, fan response and slice thickness (dual angle aluminium plates) are shown in skull-like phantoms in Fig. 8a. Complete abdomen and thorax phantoms are shown respectively in Fig. 8b and Fig. 8c (left), while inserts for low-contrast detectability, spatial resolution and edge response have been added to the thorax section in Fig. 8c (right).

CONCLUSIONS

The performance evaluation techniques for CT systems described in this paper and the modular phantoms designed to enable the important radiographic and dosimetric characteristics to be accurately measured, have proved to be useful in many practical applications. By suitable choice of evaluation insert, such investigations as comparative studies of different CT systems, acceptance testing and quality assurance can be readily undertaken.

The concept of removable inserts permits a wide range of phantom arrangements to be considered. Using this method, it should be relatively straightforward to take into account future improvements and developments in evaluation techniques by production of additional inserts.

Orientation and position checks, apparently ignored in other published and commercial phantoms, are very important and should always be included in CT phantoms. Orientation errors are relevant in the evaluation of detectability and resolution using rods, while positional errors are important when any bead-like object is being imaged. Both types of error can affect dosimetry.

Detectability and resolution test pieces using low and high contrast beads respectively, which are more applicable to the clinical situation than the conventional rod-like objects, can only be satisfactorily constructed using these types of resin-based phantom.

A survey of the performances of 29 EMI CT machines has recently been completed using the phantoms described in this paper. The following

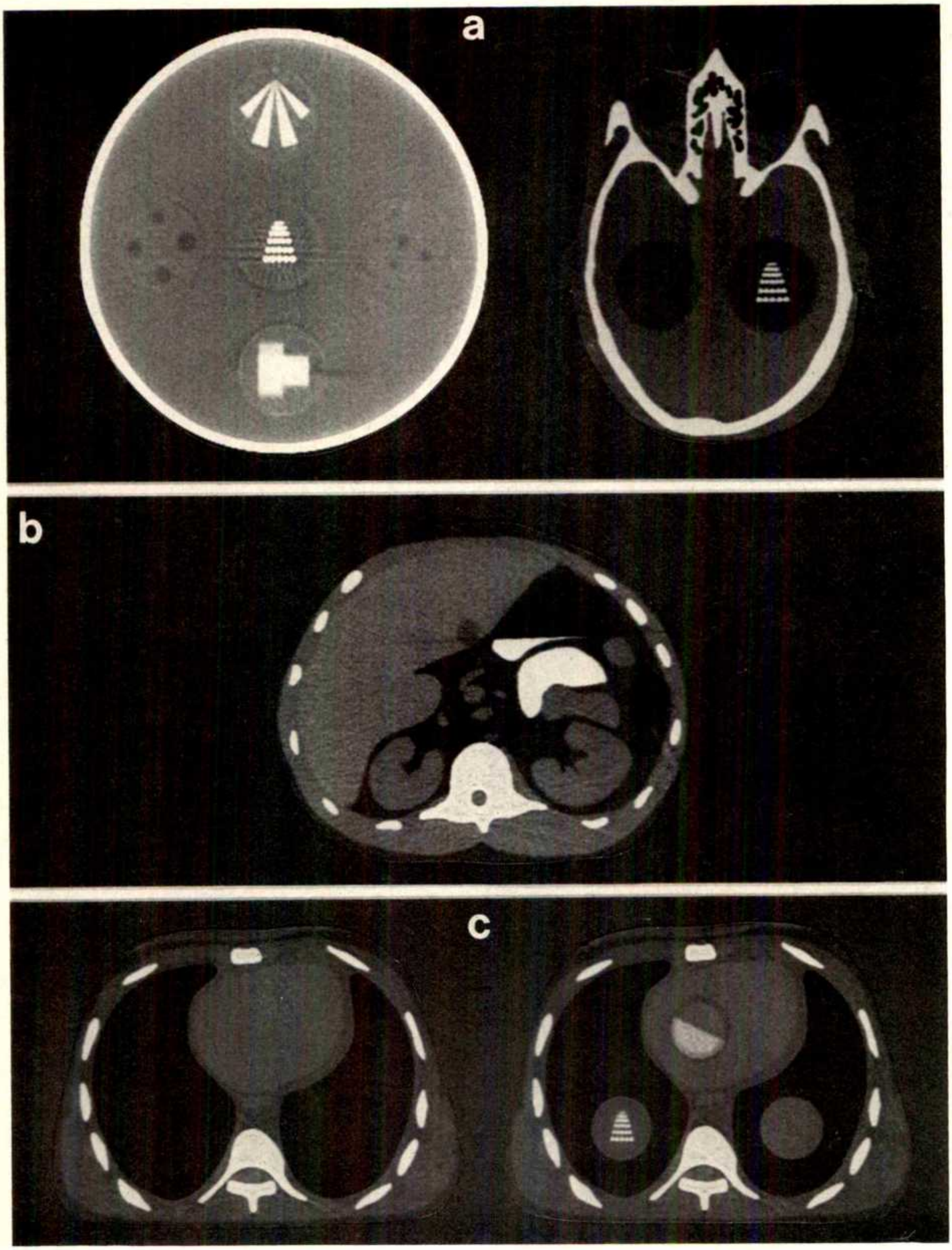


FIG. 8.

Examples of CT scans from (a) regular-geometry and anthropomorphic skull (b) abdomen and (c) thorax phantoms (window widths/centres are 200/zero except for the realistic skull which is 100/20).

paper (Speller *et al.*, 1981b) presents the results of this survey.

ACKNOWLEDGMENTS

The authors would like to record their thanks to the many colleagues who provided useful comments during the period when the phantoms described here were being designed. In particular, discussions with Dr. G. N. Hounsfield on the contents of the evaluation inserts and Dr. I. Kelsey Fry on the structure of the body sections are gratefully acknowledged. The technical assistance of Mr. A. Rickwood, Mr. R. Darlison, Mr. B. Horn and Mr. R. Spratley is acknowledged with gratitude. Mr. C. E. Temple and Mr. A. J. Coleman are thanked for their respective work on the fan response and slice thickness measurements. The help and advice of the late John Furneaux on the design of the metal moulds is acknowledged.

REFERENCES

AAPM, 1977. Phantoms for performance evaluation and quality assurance of CT scanners. *Report No. 1, American Association of Physicists in Medicine.*

BISCHOF, C. J. and EHRHARDT, J. C., 1977. Modulation transfer function of the EMI CT head scanner. *Medical Physics, 4,* 163–167.

EYCHLESHYMER, A. C. and SHOEMAKER, D. M., 1970. *A Cross-sectional Anatomy.* (Appleton-Century Crofts, New York).

GAMBARELLI, J., GUÉRINEL, G., CHEVROT, L. and MATTÈI, M., 1977. *Computerized axial tomography.* (Springer-Verlag, Berlin/Heidelberg/New York).

GOODENOUGH, D. J., WEAVER, K. E. and DAVIS, D. O., 1975. Potential artefacts associated with the scanning pattern of the EMI Scanner. *Radiology, 117,* 615–620.

HPA, 1981. Measurement of the performance of characteristics of diagnostic systems used in medicine. Part III. The physical specification of computed tomography X-ray scanners, associated measurements and their use. (Hospital Physicists' Association, London, in preparation).

JUCIUS, R. A. and KAMBIC, G. X., 1977. Radiation dosimetry in computed tomography (CT). *Proceedings of the Society of Photo-optical Instrumentation Engineers, 127* (Application of Optical Instrumentation in Medicine, VI).

JUDY, P., 1976. The line spread function and modulation transfer function of a computed tomographic scanner. *Medical Physics, 3,* 233–236.

MACINTYRE, W. J., ALFIDI, R. J., HAAGA, J., CHEBNAK, E. and MEANY, T. E., 1976. Comparative modulation transfer functions of the EMI and delta scanners. *Radiology, 120,* 189–191.

McCULLOUGH, E. C., BAKER, H. I., HOUSER, O. W. and REESE, D. F., 1974. An evaluation of the quantitative and radiation features of a scanning X-ray transverse axial tomograph: the EMI scanner. *Radiology, 111,* 709–715.

McCULLOUGH, E. C., PAYNE, J. T., BAKER, H. L., HATTERY, R. R., SHEEDY, P. F. STEPHENS, D. S. and GEDGAUDUS, E., 1976. Performance evaluation and quality assurance of computed tomography (CT) equipment with illustrative data for ACTA, Delta and EMI scanners. *Radiology,* 173–188.

ROSSMAN, K., 1971. *Image Quality. Proceedings of the AAPM Summer School, San Antonio, Texas.* Ed. D. John Wright (LHEW Publication (FDA), Rockville, Md., USA), pp. 220–281.

SPELLER, R. D., WHITE, D. R., ROTHENBURG, L., PENTLOW, K., MORGAN, T., SHOWALTER, C. and SHOPE, T. B. 1981a. An evaluation of CT systems from ten manufacturers (In preparation).

SPELLER, R. D., WHITE, D. R., VEERAPPAN, R., COLEMAN, A. J. and WALLER, P. 1981b. A survey of 29 EMI CT machines in Britain. *British Journal of Radiology, 54,* 232–240.

SYMINGTON, J., 1917. *An Atlas Illustrating the Topographical Anatomy of the Head, Neck and Trunk* (Mayne Boyd & Son., Belfast).

WHITE, D. R. and CONSTANTINOU, C., 1981. Anthropomorphic phantom materials. In *Progress in Medical Radiation Physics,* (Plenum, in press).

WHITE, D. R., MARTIN, R. J. and DARLISON, R., 1977. Epoxy resin based tissue substitutes. *British Journal of Radiology, 50,* 814–821.

WHITE, D. R. and SPELLER, R. D., 1980. The measurement of effective photon energy and "linearity" in computerized tomography. *British Journal of Radiology, 53,* 5–11.

Book review

Review of Medical Terminology. By Mary E. Kinn. 1980 pp. 144, illus. (George Thieme, Stuttgart; Thieme-Stratton, New York). DM 19.80.
ISBN 3-13-0003-01-0

New entrants to the sphere of health care, including trainee radiographers, find the vocabulary of medical terminology a difficult initial hurdle. There are a variety of compact dictionaries and glossaries which provide sources for ready reference and with experience mastery of the new language is ultimately achieved.

This book has been created to provide a test of the level of expertise achieved and is based on experience of medical terminology classes held for broad audiences. It is presented in twelve chapters, the first two being introductory and the remainder related to specific body systems. Each comprises a few brief paragraphs outlining the subject matter followed by up to a hundred multiple choice questions. The first relate to line diagrams of the subject matter with numbered elements which must be matched with a list of names. The volume is designed for use alone or in conjunction with a standard text book of medical terminology. The author has used three such books to which references are made in the answers.

All in all the material is presented well but inevitably the spelling is American. It will appeal to those who find practice with multiple choice questions a useful adjuvant to learning. It might be a useful addition to the libraries of radiography schools.

J. ROYLANCE.

1981, *British Journal of Radiology*, *54*, 232–240

A survey of 29 EMI CT machines in Britain

By *R. D. Speller, Ph.D., †D. R. White, Ph.D., ‡R. Veerappan, B.Eng., *A. J. Coleman, M.Sc. and ‡P. E. Waller, M.A.

*Department of Physics as Applied to Medicine, Middlesex Hospital Medical School, Cleveland Street, London W1P 6DB
†Radiation Physics Department, St. Bartholomew's Hospital, 13 Bartholomew Close, London EC1A 7BE and
‡EMI Medical Ltd., 248 Blyth Road, Hayes, Middlesex

(*Received December 1979 and in revised form August 1980*)

Abstract

During 1978/79 a survey was made of the performance characteristics of 29 EMI brain and body CT scanners in Britain. Comparative data on such performance parameters as noise, uniformity of CT numbers, low-contrast detectability, resolution, modulation transfer function (MTF) and effective photon energy were measured using a set of regular-geometry and anthropomorphic phantoms. In addition, dose profiles were obtained for a single slice using TLD and film. The results of the survey are presented; the dependence of the performance characteristics on the types of machines surveyed and the operating modes employed is discussed.

During the period October 1978 to January 1979, a detailed series of radiographic and dosimetric performance measurements was made on 29 EMI CT scanners. Both brain and general-purpose scanners were surveyed, located at 26 sites in England, Scotland and Wales, including installations at Birmingham, Cardiff, Glasgow, London and Manchester.

The aims of the survey were threefold:

(i) To establish the spread in the important performance characteristics of CT machines in use in hospitals in order to provide a useful data base for evaluation of the performance of individual scanners.

(ii) To measure the performance characteristics with regular-geometry and anthropomorphic phantoms in order to provide comparative data under both idealized and realistic conditions.

(iii) To investigate the variation in the performance of each type of scanner when used in each of its operating modes, so that the most appropriate modes could be established for given imaging tasks.

Brief descriptions are given of the different types of CT machines and their operating modes, the performance parameters considered and the methods of evaluation, together with an account of the results obtained. It must be stressed that except for one factory-based scanner, the machines tested were all in clinical use at the time of the survey. In order that the results should be a true reflection of the performance of CT machines in Britain, no attempt was made to modify or improve the performance of any machine immediately before the tests.

CT Machines and Operating Modes

The types of EMI CT scanners evaluated were chosen so as to be representative of the range of machines in operation in Britain during the survey period. These were predominantly the CT1010 brain and the CT5005 general-purpose body machines, but an older brain scanner, the CT1000, was also included. It is important to note the basic differences between these systems.

CT1000

This system is similar to the original Mk I brain scanner (Hounsfield, 1973) but has an improved gantry mechanism. A water-box is employed and the X-ray beam scans over 180° with 1° indexing. Three sodium iodide/photomultiplier detectors are used and two contiguous slices are imaged per scan, with slice thicknesses of either (nominally) 8 or 13 mm. The time needed for scan plus processing is 270–396 seconds for 160 × 160 matrix reconstructions.

CT1010

Developed from the Mk I and CT1000, this brain scanner uses, instead of a water-box, carbon correction wedges to define scan fields of 180, 210 and 240 mm diameter. The X-ray beam has 3° indexing over either 180° or 240°. Seventeen sodium iodide/photomultiplier detectors are used and two contiguous slices are imaged per scan, each nominally of thickness 10 mm (the comparable version sold in the USA has 2×8 mm slices). Scan times from 60–240 s may be selected, with processing times for two slices of 27 s (160×160 matrix) or 162 s (320×320 matrix). Optional narrow collimators are available (CT1010(NC)), giving nominal slice thicknesses of 5 mm. The CT1010 group of scanners included two CT1007 and three CT1010S machines, both older scanners updated to the CT1010 specification. The

CT1007 is the name given to an updated Mk I scanner (in the USA this update is designated CT1005), while the CT1010S is an updated CT1000.

CT5005

A general-purpose body scanner, developed from the original CT5000 machine (Kreel, 1977), this scanner has aluminium correction wedges to define scan fields of 240, 320 and 400 mm diameter. The X-ray beam has 10° indexing over 180°. Thirty-one sodium iodide/photomultiplier detectors are used and one 13 mm (nominal) slice is imaged per scan. Scan times of 27 or 80 s may be selected, with additional processing times of 22 s (160×160 matrix) or 85 s (320×320 matrix). A high-resolution option (CT5005(HR)) is available, with improved resolution over the central region of the scanned area corresponding to half the normal fields of view. This is available with 5, 10 or 13 mm slice thicknesses.

The 29 scanners evaluated in this survey are as follows, with the number of each type surveyed given in parentheses. CT1000 (1); CT1010 (12); CT1010(NC) (1); CT5005 (14); CT5005(HR) (1). The operating modes used with these machines are shown in Table I, together with details of matrix size, process code, angular rotation and nominal scan times.

It can be seen that 22 different operating modes have been considered, designated by four or five characters. In general, the designation indicates the matrix size (160 or 320), the scan time (N=normal; S=slow) and, where appropriate, the process code (F or C). In the case of the CT1010 machines operating in the overscan mode, when the angular rotation is increased from 180° to 240°, the letter "A" is introduced. It must be emphasized that these designations cannot be used on their own and must always be linked with the machine and scan type being evaluated.

In general, during "brain" scanning, machines were operated at 120 kV and 33 mA, while for thorax and abdomen scanning (referred to as "body" scanning in this study) 140 kV and 28 mA was used. During high-resolution and narrow-collimator scanning, the latter high kilovoltage option was adopted. Any other departures from the general

TABLE I

THE OPERATING MODES USED IN THE SURVEY

Machine	Scan type	Operating modes				
		Designation	Matrix	Process code*	Angular rotation	Nominal scan time (Seconds)
CT1000	Brain	160N	160 × 160	—	225°	300
		160S	160 × 160	—	225°	396
CT1010	Brain	160N	160 × 160	—	180°	60
		160S	160 × 160	—	180°	240
		160AS	160 × 160	—	240°	80
		320N	320 × 320	—	180°	60
		320S	320 × 320	—	180°	240
		320AS	320 × 320	—	240°	80
CT1010(NC)	Brain	320AS	320 × 320	—	240°	80
CT5005	Brain	160N	160 × 160	HP	180°	27
		160S	160 × 160	HP	180°	80
		320FN	320 × 320	F	180°	27
		320CN	320 × 320	C	180°	27
		320FS	320 × 320	F	180°	80
		320CS	320 × 320	C	180°	80
CT5005(HR)	Brain	320FS	320 × 320	F	180°	80
		320CS	320 × 320	C	180°	80
CT5005	Body	160N	160 × 160	HP	180°	27
		320FN	320 × 320	F	180°	27
		320CN	320 × 320	C	180°	27
CT5005(HR)	Body	320FS	320 × 320	F	180°	80
		320CS	320 × 320	C	180°	80

*HP: High precision; F: Full process; C: Combined angle process.

rules were due to local preferences, and performance data from these machines are, where relevant, mentioned separately in the "Results" section.

All of the data quoted in this paper for the dual-slice brain scanners were derived from the "A" slice images. Only a limited number of "B" slice images were evaluated in order to confirm the validity of this approach.

METHODS OF EVALUATION

A single set of phantoms was used during this study to evaluate each of the 29 CT machines and they were set up exactly as each centre prepared their patients for scanning. The phantoms fall into two categories, namely circular water-filled Perspex containers and a range of solid, regular-geometry and anthropomorphic phantoms. Full details of the solid phantoms and the array of performance inserts that fit into them are given in the preceding paper (White *et al.*, 1981).

Nine categories of performance parameters were evaluated during the survey and they are listed in

TABLE II

EVALUATION PROCEDURES

Parameter	Performance insert	Phantoms used (R: Regular; A: Anthropomorphic)		Insert locations	Comments
		Type	Fig.		
Alignment	Aluminium pin, 3.17 mm diameter	Skull (R) Body (R)	1a 1b	2 8	Subjective analysis of enlarged (160 × 160) segment of 320 × 320 matrix scan (window width/centre: 1/15)
Slice thickness	Dual inclined (30° and 45°) aluminium plates, 0.72 mm thick	Skull (R) Body (R)	1a 1b	1 and 3 6 and 10	Pair of aluminium plates inclined at 45° not available for survey (see preceding paper for details)
Noise	—	Circular water-filled Perspex containers (20 and 33 cm diameter, 10 cm thick)		—	Central, circular areas, 100 pixel radius assessed
Uniformity of CT numbers	—	As for noise		—	Circular areas, 20 pixel radius assessed at co-ordinates (160 × 160 matrix) (80, 80), (40, 80), (80, 120), (120, 80), (80, 40)
Low contrast detectability	Polystyrene rods and beads, 1–10 mm diameter, in increments of 1 mm	Skull (R) Body (R) Skull (A) Thorax (A)	1a 1b 1c 1d	1, 3 and 5 13 and 14 15 18	Subjective assessment by four independent observers
Spatial resolution	Arrays of rods and beads of cortical bone substitute, 0.5–2.5 mm diameter in increments of 0.25 mm	Skull (R) Body (R) Skull (A) Thorax (A)	1a 1b 1c 1d	2 8 and 9 16 19	Subjective assessment by four independent observers.
Modulation transfer function	Perspex edge	Skull (R) Body (R) Thorax (A)	1a 1b 1d	3 and 4 11 17	Evaluated using the technique of Judy (1976).
Dose to patient	TLD-100 LiF ribbons in Perspex holders	Skull (A) Thorax (A)	1f 1g	21 + six peripheral sites 22 + eight peripheral sites	Dose profiles assessed from TLD, calibrated with X rays having effective energy 79 keV.
Effective energy and linearity of CT numbers	"KeV liquids"	Skull (R) Body (R)	1a 1b	2 8	See White and Speller, 1980.

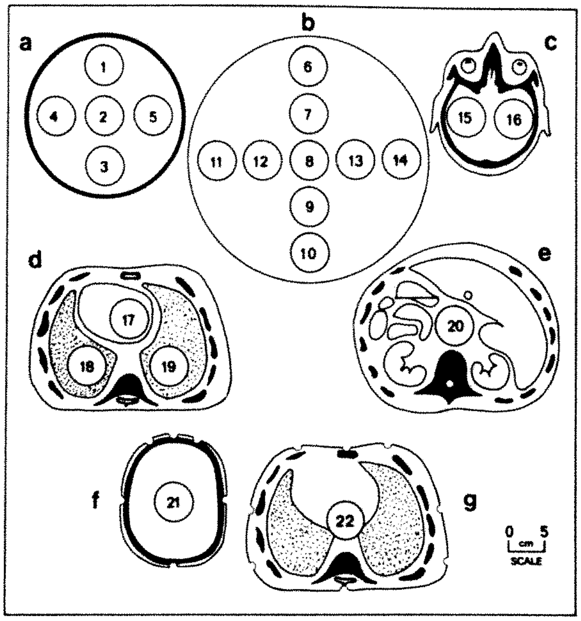


Fig. 1.

The range of solid epoxy-resin-based phantoms used in the survey.

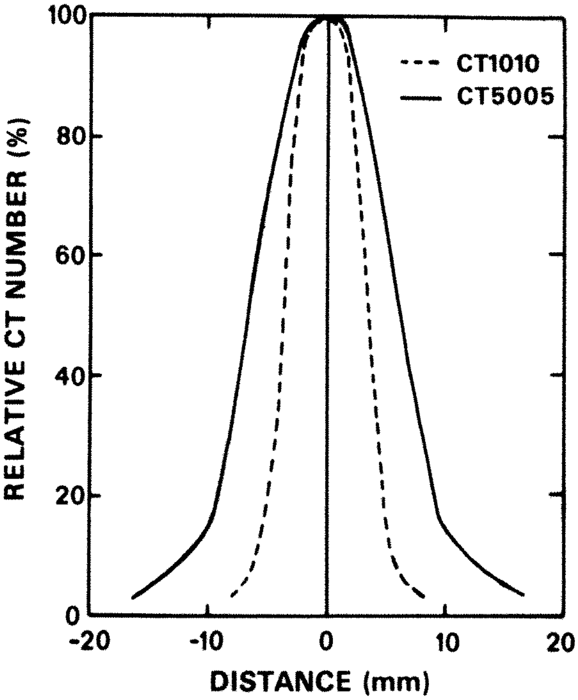


Fig. 2.

Typical slice sensitivity profiles.

TABLE III

Summary of slice thickness results

Machines		Scan type	Mean slice thickness (mm)	
No.	Type		Top	Bottom
12	CT1010	Brain	7.7	7.6
1	CT1010(NC)	Brain	4.4	4.1
13	CT5005	Brain	12.8	12.6
1	CT5005(HR)	Brain	3.9	4.3
12	CT5005	Body	12.0	12.4
1	CT5005(HR)	Body	3.3	3.8

Table II together with descriptions of the performance inserts that were used and their locations in the phantoms employed (Fig. 1). For more detailed information on the parameters given in Table II, the reader should refer to the preceding paper.

In addition to the nine basic parameters, a subjective assessment of image quality and artefacts was undertaken by analysing the images obtained from the anthropomorphic skull phantom (Fig. 1c). This assessment required comments from independent observers who viewed the displayed images.

Throughout the survey, brain scanning procedures were evaluated with the 20 cm diameter regular-geometry or anthropomorphic skull phantoms, while body scanning was evaluated with the 33 cm diameter regular-geometry, the realistic thorax or abdomen phantoms.

Results

The principal results of this study are presented in Tables III and IV and Figs. 2–6. The format of the five sets of graphs given in Figs. 3 and 4, with the common abscissae, has been chosen so that any correlations between the six performance parameters (noise, uniformity of CT numbers, detectability, resolution, MTF, patient dose) may be highlighted.

Repeat measurements of specific performance parameters were not generally undertaken on each machine during the survey, so standard errors are not readily available. However, measurements on a few selected machines have indicated that the standard errors on the nine parameters considered are smaller than the standard deviations quoted here.

For reliable results it was imperative that the position of the image plane with respect to the optical marker was accurately known for each scanner tested. Measured mean image-marker distances of 47.4±2.1 mm for the "A" slice of the CT1010 machine and 181.4±1.5 mm for the single slice CT5005 machine were recorded. These variations from the quoted nominal values of 45 and 180 mm respectively are large enough to produce problems

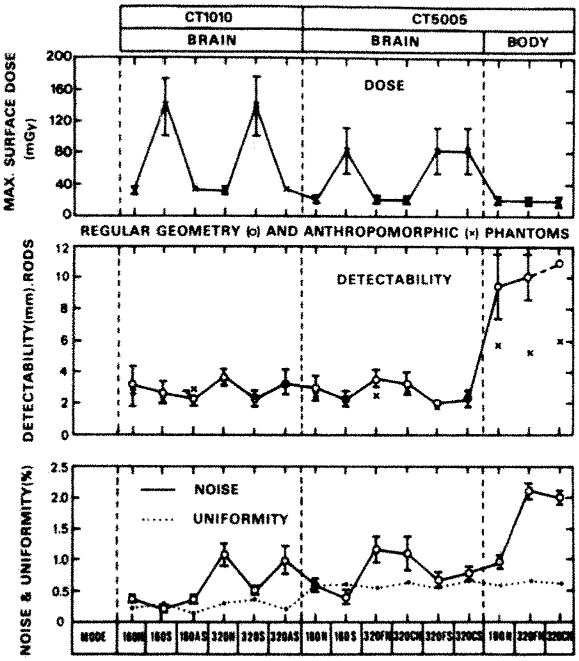


FIG. 3.

Results for noise, uniformity of CT numbers, low-contrast detectability and maximum surface dose.

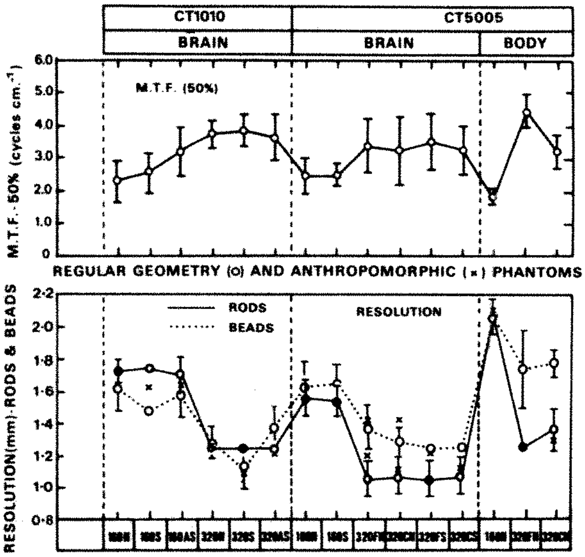


FIG. 4.

Results for spatial resolution and 50% MTF.

with small bead-like test pieces, when accurate positional checks are essential (White *et al.*, 1981).

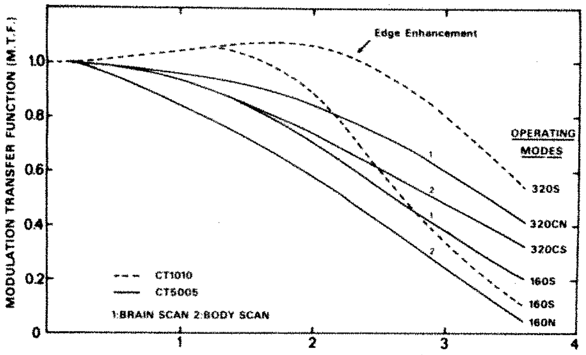


FIG. 5.

Typical MTF curves.

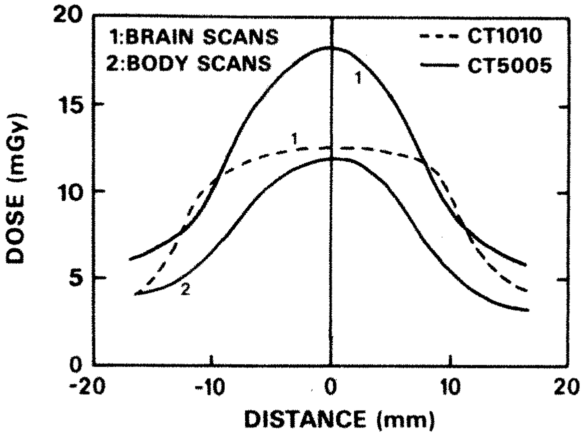


FIG. 6.

Typical mid-point, single-slice dose profiles.

Alignment checks, assessed subjectively from the streaking artefacts produced by a high-contrast aluminium pin, showed that three scanners (one brain and two body machines) had graticule misalignments.

Slice thickness is summarized in Table III. The mean values for measurements at the top and bottom (locations one and three or six and ten) of solid regular-geometry phantoms are listed for each group of scanners. The group of CT1010 machines gave results in close agreement, with small standard deviations (~6%) and similar values of slice thickness at the top and bottom of the 20 cm diameter phantom. The CT5005 group gave larger standard deviations (~9%) when evaluated in the brain mode, due probably to their more complicated collimating systems being difficult to adjust. The results for the body mode with the 33 cm diameter phantom gave slice thicknesses at the top that appeared to be slightly smaller than at the bottom. Two typical profiles of slice sensitivity obtained during this part of the analysis from two well-adjusted machines are shown in Fig. 2. Small but significant deviations from these curves, indicating that the beam collimator and detector collimator are not exactly in line, were noted in one brain and seven body machines.

Noise is presented in the lower graph in Fig.3 for 15 of the 22 operating modes. For each group of noise determinations, mean values and standard deviations from the mean are plotted, with the largest noise values being recorded for the CT5005 machines used for body scanning. As expected, all of the 320 × 320 matrix scans are noisier than the 160 × 160 matrix scans, as are the "normal" (N) scans compared with the "slow" (S) scans. Brain scanners gave marginally less noise than the body machines used in the same mode. The high-resolution options gave much noisier images than any other machine or operating mode. For CT5005(HR), noise values of 2.7% and 6.0% were recorded respectively for brain and body scanning with 320 × 320 matrix reconstructions. For CT1010(NC), noise values of 0.6% were recorded for comparable modes. There would appear to be little advantage in using the 240° scan mode in CT1010 scanners (160AS, 320AS) just to improve the noise in the image when movement of the patient is not a problem.

Uniformity of CT numbers across the scan area is shown as mean values in the lower section of Fig. 3. The average results for the body scanners were higher than the average values for the brain machines, with operating mode having little effect on the values recorded for a given type of machine. It is interesting to note that 240° scans (160AS, 320AS) do improve uniformity as would be expected from the correction procedure used in the reconstruction of these images. Only in a few instances (*e.g.* certain 160S brain scans) did the uniformity values exceed the noise values, implying that its non-uniformity was recognizable in the scanned image. Standard deviations varied from 23.5–61.5%.

Low-contrast detectability is plotted in the central graph of Fig. 3, for the same 15 operating modes as used for the graphical representation of the noise data. Mean values of the minimum detectable diameters observed are plotted together with indications of the standard deviations. The results for brain scanning are remarkably uniform, about 2–4 mm, although it should be noted that this order of variation does produce a noticeable change in image quality. Poorer detectabilities were obtained with body scanning, although the smaller anthropomorphic thorax phantom (Fig. 1d) yielded better values than the solid regular-geometry phantom (Fig. 1b). Minimal differences were observed between the "F" and "C" process codes of the CT5005 scanner. The data for CT1010(NC) and CT5005(HR) were in the upper, poorer detectability region of the relevant spreads shown in the graph, while the results for the CT1000 machine were in the lower region indicating improved detection. The shape of the graphs shown in Fig. 3 for detectability and noise match each other closely over all the operating modes evaluated. This illustrates the strong noise dependence of this parameter, because as the noise increases the image quality deteriorates, resulting in a corresponding increase in the value of the minimum detectable diameter of the polystyrene rods. Even at 3% contrast, detectability is a noise-limited process.

Spatial resolution in the form of minimum resolvable diameter arrays of high-contrast rods and beads is plotted for the same 15 operating modes in the lower section of Fig. 4. As for the previous parameter, mean values and their associated standard deviations are plotted. With brain scanning, if the mean values of resolution for rods are considered, the best resolutions occur with the 320 × 320 matrix and the general purpose machines for both regular geometry and realistic phantoms. Mean values of about 1.05 mm for the body machines compare with about 1.25 mm for the brain machines.

TABLE IV

SUMMARY OF EFFECTIVE PHOTON ENERGIES, LINEARITY DATA AND MEAN CT NUMBERS FOR WATER AND AIR

Machines		kV/mA	Scan type	Mean effective energy (keV)	Mean CT numbers		$\mu = a_1$ (CT No.) $+ a_0$	
No.	Type				Water	Air	a_0	a_1
11	CT1010	120/33	Brain	70.4	−1.8	−1000.8	0.192	1.90×10^{-4}
1	CT1010(NC)	140/28	Brain	76	−3.0	−984.6	0.187	1.88×10^{-4}
13	CT5005	120/33	Brain	70.4	0.7	−485.4	0.192	4.05×10^{-4}
1	CT5005(HR)	140/28	Brain	76	−11.6	−485.2	0.191	3.97×10^{-4}
14	CT5005	140/28	Body	79.2	0.5	−467.9	0.184	3.97×10^{-4}
1	CT5005(HR)	140/28	Body	80	0.8	−470.6	0.182	3.89×10^{-4}

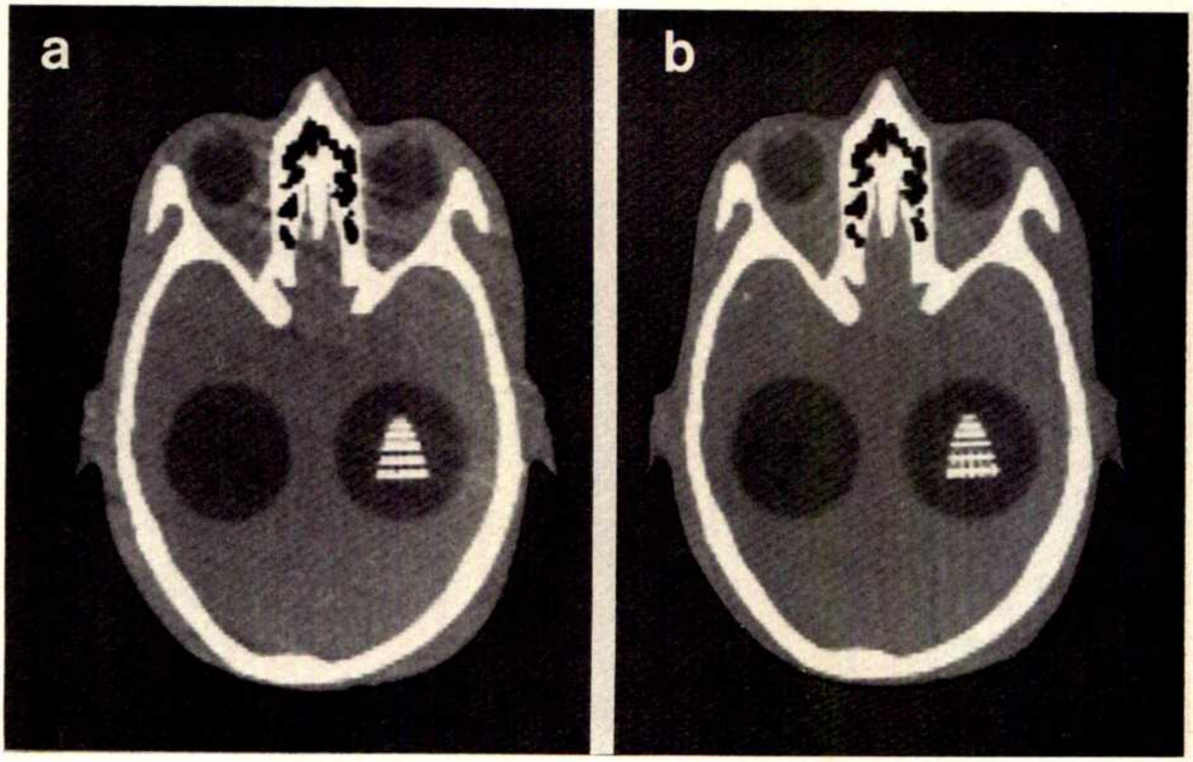
Larger standard deviations were observed with beads due to their strong positional dependence along the axis of the scanners, particularly with the CT1010 which has a smaller slice thickness. No significant improvement in resolution was recorded in changing from "normal" (N) to "slow" (S) scan times, or, in the case of body scanners, in changing from "F" to "C" process codes. The CT1010(NC) and CT5005(HR) machines had resolutions of 1.25 and 0.75 mm respectively for rods. The CT1000 machine gave similar results to the quoted data for the CT1010 machines.

Modulation transfer function as spatial frequency corresponding to the 50% MTF values (cycles cm^{-1}) is presented in the upper section of Fig. 4 and correlates well with the spatial resolutions shown in the lower section. The mean values and standard deviations are plotted for each group of determinations. The 50% MTF graph is an inverted image of the resolution graphs, confirming the conclusions regarding scan times and process codes given for the resolution results. The improved resolution noted with the rod patterns for CT5005 brain scans compared with CT1010 scans is not so obvious with the 50% MTF curve due to the larger standard deviations recorded for the body machines. For brain scanning with the 320 × 320 matrix, the average 50% MTF was about 3.7 cycles cm^{-1} for brain and 3.3 cycles cm^{-1} for body scanners. For the high-resolution body scanner the comparable 50% MTF value was about 9.1 cycles cm^{-1}. A complete set of MTF curves obtained from well-adjusted brain and body machines under a selection of operating modes is shown in Fig. 5.

Dosage in the form of maximum surface dose for single-slice scans is depicted in the upper graph of Fig. 3. Again, means and standard deviations are indicated. Scan times were checked during each dosimetry run and found to have maximum discrepancies of 9.4%. Mean doses are generally in the range 20–40 mGy, although the two slowest scan times for brain scans give mean values of about 140 mGy and 80 mGy. The relevant dose data given recently by Hobday and Parker (1978) and Wall *et al.* (1979) appear to fit reasonably well within the spread of results given here. The large standard deviations recorded in Fig. 3 for the high doses require some explanation. For the CT1010 machines, doses for the 160S and the 320S scans appear to be dependent upon the X-ray tube life. In the group of three machines assessed, tube lives were 13, 48.5 and 301 hours, while the maximum surface dose rates were respectively 6.6, 5.8 and 3.7 $mGys^{-1}$. This reduction in dose with increasing tube life, only apparent for this slow scan time, requires more investigation. For the CT5005 brain scans 160S, 320S and 320CS, the large standard deviations were due to one machine in the group of four having, as yet unexplained, a dose rate 1.8 times greater than the others in the group. Brain scans with CT1010(NC) and CT5005(HR) machines gave maximum surface doses of 155 mGy and 104 mGy respectively, while for body scanning the CT5005(HR) gave a maximum dose of 80 mGy. The maximum surface dose recorded for the CT1000 machine was 16 mGy. Typical dose profiles for brain and body scanners measured at the centre of the anthropomorphic phantoms are shown in Fig. 6.

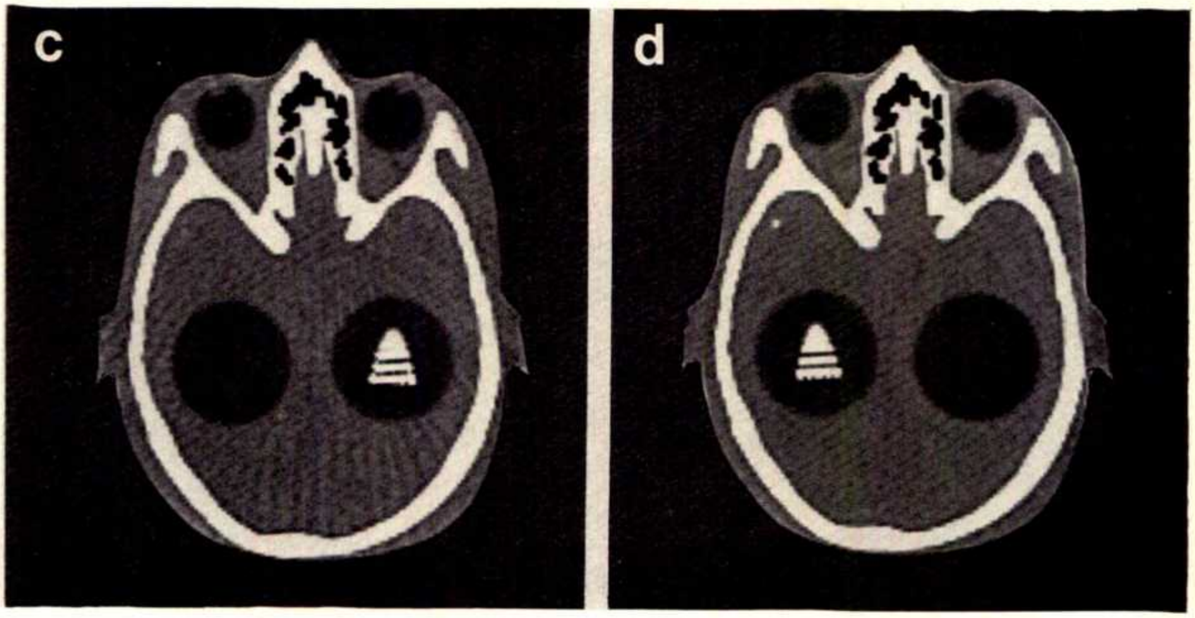
Effective energy and linearity of CT number is summarized in Table IV together with the mean CT numbers for water and air at the centre of the solid regular-geometry phantoms. The table indicates the number of machines considered in each category and shows mean values recorded. The 24 brain and general-purpose scanners operating at the standard 120 kV/33 mA settings and used for brain scanning had E_{eff} in close agreement in the range 70–71 keV. The CT1000 scanner surveyed which was also operated at 120 kV/33 mA had an E_{eff} of 71 keV. A brain machine operating at 119 kV/32 mA and not included in the table had an E_{eff} of 69 keV, and a CT5005 machine operating at 140 kV/28 mA for brain scanning, again not included in the table, gave an E_{eff} of 76 keV. An interesting difference in effective energy was evident between brain and body scans obtained with machines operating at 140 kV/28 mA. Brain scans from scanners using the high resolution and narrow collimator options gave E_{eff} of 76 keV while body scans from the group of fourteen CT5005 machines gave a higher mean value of 79.2 keV. This was due to the increased beam hardening in the larger phantom employed for the body scans. The relationship between μ and CT number for the 29 machines tested were essentially linear with correlation coefficients consistently being about 0.999. When the different CT number scales are taken into consideration, the values obtained for the constant a_1, which relates to the contrast characteristics of the scanners, are in close agreement.

Finally, in Fig. 7 a set of scans is shown to illustrate how some of the performance parameters discussed here correlate with subjective image quality in anthropomorphic phantoms. The figure shows both good and bad 160 N brain scans for body (Fig. 7a, b) and brain (Fig. 7c, d) machines operating at 120 kV and 33 mA. Low-contrast detectability, spatial resolution (rods) and maximum surface dose are given for each image. It can be seen



LCD: 3 mm; SR: 1.5 mm; D: 17.3 mGy.

LCD: 1 mm; SR: 1.5 mm; D: 21.7 mGy.



LCD: 4 mm; SR: 1.75 mm; D: 34.5 mGy.

LCD: 2 mm; SR: 1.75 mm; D: 38.7 mGy.

FIG. 7.

An illustration of the subjective assessment of images from machines having good and poor radiographic performance. (a and b) whole-body scanners (window/level: 100/20); (c and d) brain scanners (widow/level: 200/40). *Abbreviations:* Low-contrast detectability (LCD); spatial resolution (SR); maximum surface dose (D).

that for machines of the same type the detectability is governed by noise and artefacts generated in the image, and that despite a two-fold increase in dose the brain scanner images have poorer characteristics. Similar data from the larger thorax (Fig. 1d) and abdomen phantoms (Fig. 1e) are also available.

CONCLUSIONS

The study has provided a comprehensive set of performance data for the first and second generation EMI CT machines; the measuring techniques were such that the data may be applied with reasonable confidence to clinical use. In particular, the tabular and graphical presentations of the data should enable the performance characteristics of any improvements to these systems to be readily assessed.

Seven general conclusions are apparent from the results:

(1) Close agreement between machines of the same type was noted for many performance parameters. These included slice thickness, uniformity of CT numbers, effective photon energy and linearity of CT numbers. However, certain parameters such as dose and 50% MTF are less consistent.

(2) There was a wider spread in the performance data for the CT5005 than for the brain machines, an indication, perhaps, of the increased complexity of the general purpose machine and of the need for regular quality assurance.

(3) For brain scanning, the body scanner, if well maintained, produces images as good as, if not better than, the CT1010, in a shorter time and with a smaller maximum surface dose to the patient.

(4) Differences in performance between the "F" and "C" process codes, available with the body machines, appear to be minimal, indicating that the use of the "F" code, which increases processing time from 50 to 85 seconds, is not justified unless good peripheral detail is required.

(5) Again, in the absence of patient movement, use of the overscan (240°) facility in brain machines does not appear to produce a significant improvement in performance, except with regard to uniformity of CT numbers.

(6) Machines with the high-resolution option give greatly improved spatial resolution at the expense of decreased detectability and increased dose to the patient.

(7) A correlation was apparent between the results for the edge derivation of 50% MTF and resolution from high-contrast rod patterns. lending confidence to the use of these patterns for the rapid specification of resolution. A further correlation was noted between detectability at 3% contrast and noise.

ACKNOWLEDGMENTS

We would like to record our gratitude for the help given by the many radiologists, physicists and radiographers at the 26 sites visited; without this support, the survey would not have been possible. We also wish to express our thanks to EMI (Medical) Ltd. for providing the finance for travel and subsistence, and for giving financial support to one of us (A.J.C.) which enabled him to spend seven months on the initial analysis of data. Mr. B. F. Wall and the staff running the National Radiological Protection Boards TLD department in Glasgow provided invaluable advice and assistance. Mr. C. K. Showalter, Dr. T. B. Shope and their colleagues at the Bureau of Radiological Health, Washington, USA, are thanked for their collaborative work on the TLD calibrations. The help and encouragement given by Mr. R. H. Davies, Mr. D. A. C. Green, Dr. J. N. A. Ridyard, Mr. T. H. E. Bryant and Dr. W. E. Liversage is gratefully acknowledged.

REFERENCES

Hobday, P. and Parker, R. M., 1978. Radiation exposure to the patient in computerized tomography. *British Journal of Radiology*, *51*, 925.

Hounsfield, G. N., 1973. Computerized transverse axial scanning (tomography) Part I. Description of system. *British Journal of Radiology*, *46*, 1016–1022.

Judy, P., 1976. The line spread function and modulation transfer function of a computed tomographic scanner. *Medical Physics*, *3*, 233–236.

Kreel, L., 1977. Computerized tomography using the EMI general purpose scanner. *British Journal of Radiology*, *50*, 2–14.

Wall, B. F., Green, D. A. C. and Veerappan, R., 1979. The radiation dose to patients from EMI brain and body scanners. *British Journal of Radiology*, *52*, 189–196.

White, D. R. and Speller, R. D., 1980. The measurement of effective photon energy and "linearity" in computerized tomography. *British Journal of Radiology*, *53*, 5–11.

White, D. R., Speller, R. D. and Taylor, P. M., 1981. Evaluating performance characteristics in computerized tomography. *British Journal of Radiology*, *54*, 221–231.

1981, *British Journal of Radiology*, *54*, 241–244 MARCH 1981

Hydatid disease: the value of whole-body screening by scintigraphy with technetium-99m-labelled red blood cells

By D. Front, M.D., Ph.D. and Ora Israel, M.D.

Division of Nuclear Medicine, Rambam Medical Center and Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

(Received April 1980 and in revised form July 1980)

ABSTRACT

Whole-body scintigraphy with ^{99}Tc^{m}-labelled red blood cells was performed in eight patients with hydatid disease. There was good correlation between these studies and other diagnostic procedures which included radiocolloid liver scintigraphy, liver ultrasound, body computed tomography and chest radiography. Whole-body scintigraphy with ^{99}Tc^{m}-labelled red blood cells appears suitable for screening patients with hydatid disease, many of whom have multiple organ involvement.

Hydatid disease is a widespread parasitic infection caused by the larval form of *Echinoccocus granulosus*. It is prevalent in sheep-raising countries (Reeder, 1970) where sophisticated and expensive diagnostic modalities are sometimes not readily available. A simple screening examination seems necessary in order to indicate the involvement of various organs by the disease and select patients where further studies need to be performed.

We report here our experience in using whole-body scintigraphy with ^{99}Tc^{m}-labelled red blood cells as a screening procedure in patients with echinoccocosis.

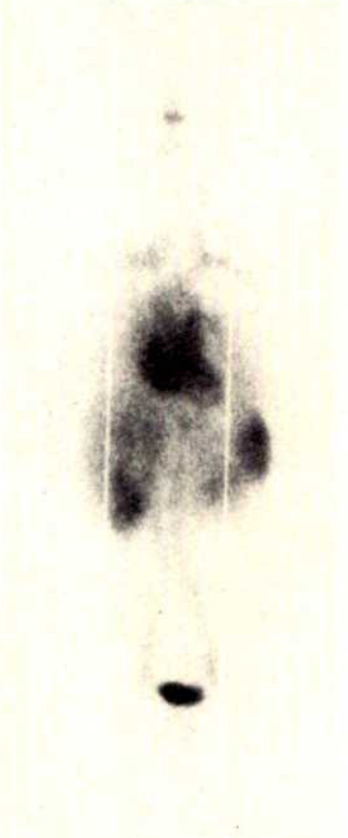
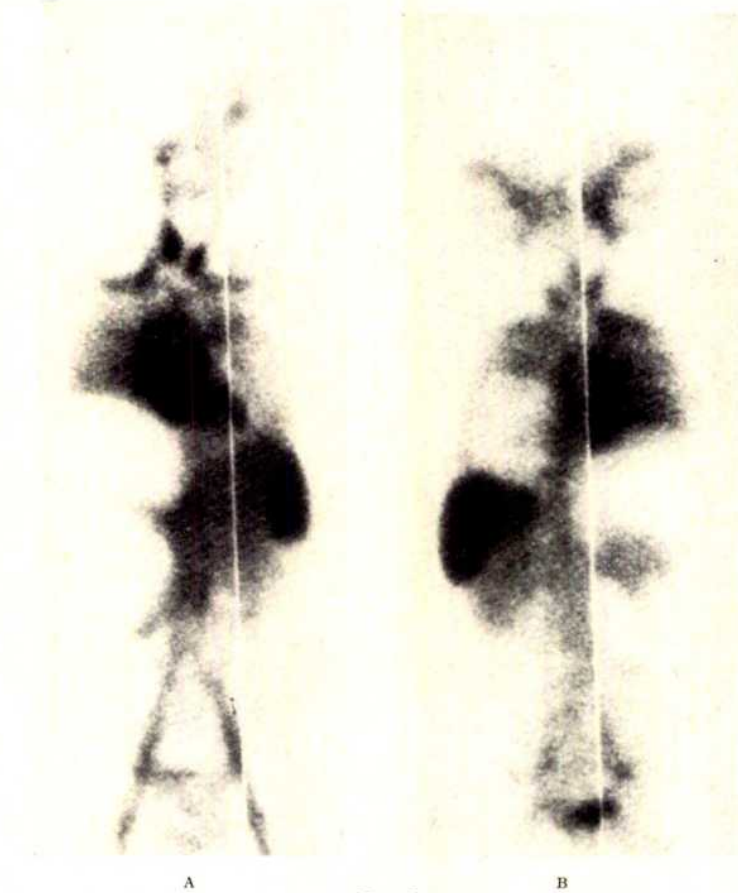


FIG. 1.

Normal whole-body scintigram with ^{99}Tc^{m}-labelled red blood cells.



A B

FIG. 2.

Whole-body scintigraphy with ^{99}Tc^{m}-labelled red blood cells in Case 1 (Table I). (A) Anterior view. (B) Posterior view. Two cysts in liver and lung are demonstrated.

TABLE I

CLINICAL, SCINTIGRAPHIC AND RADIOGRAPHIC FINDINGS IN EIGHT PATIENTS WITH ECHINOCCOCOSIS

		Number of lesions found by various methods												
		Radiocolloid liver, spleen scan		Abdominal ultrasound		Computed tomography				^{99}Tc^{m}-labelled red blood cells				
Patients	Clinical data	liver	spleen	liver	spleen	liver	spleen	lung	Chest X-rays	liver	spleen	lung	Total	Number found at surgery
1. Male age 30	Family infected, abdominal pain, hepatomegaly, Cassoni – negative	2	0	2* (1)	0	2	0	1	1	2	0	1	3	NP
2. Male age 54	Cough, abdominal pain, hepatosplenomegaly	2	1	2	1	NP	NP	NP	2	2	1	2	5	5
3. Male age 15	Hydatid disease in members of family, Cassoni – positive	1	0	1	0	1	0	1	1	1	0	1	2	2
4. Female age 32	Cough, chest pain, hepatomegaly, Cassoni – positive	2	0	2	0	2	0	1	1	2	0	1	3	3
5. Male age 62	Operated in past for echinoccocus of liver and lung, Cassoni – positive	0	0	0	0	NP	NP	NP	1	0	0	1	1	NP
6. Male age 45	Abdominal pain, hepatomegaly, Cassoni – positive	1	0	1	0	NP	NP	NP	0	1	0	0	1	1
7. Female age 42	Abdominal pain, fever, Cassoni – positive	1	0	1	0	NP	NP	NP	0	1	0	0	1	1
8. Female age 13	Hydatid disease in members of the family, Cassoni – positive	0	0	0	0	NP	NP	NP	1	0	0	1	1	1

NP Not performed.
* One cyst evident on ultrasound, the other suspected.

MATERIALS AND METHODS

Eight consecutive patients with hydatid disease were included in the study. All underwent liver scintigraphy with ^{99}Tc^m-sulphur colloid or ^{99}Tc^m-phytate, as well as whole-body scintigraphy with ^{99}Tc^m-labelled red blood cells. Each patient underwent one or more additional imaging procedures including liver ultrasound, lung and abdominal computed tomography and chest radiography; see Table I.

In six patients diagnosis was based on material obtained during operation; in two (Nos. 1 and 5 in Table I) the combination of clinical findings and diagnostic procedures was highly suggestive.

Labelled red blood cells were prepared either *in vitro* with a commercial kit or by *in-vivo* labelling. Each study utilized 555 MBq (15 mCi) of the radiopharmaceutical and was performed with a gamma camera and whole-body scanning table. Thirty to forty minutes were required to obtain whole-body scintigrams in the anterior and posterior views. Whole body radiation dose is 0.73 μGy/MBq (2.7 mrad/mCi) (Ryo *et al.*, 1974).

RESULTS

A normal whole-body scintigram with ^{99}Tc^m-labelled red blood cells is shown in Fig. 1. As the liver, spleen and lungs are well visualized, avascular lesions can be detected in these organs. The relevant clinical, scintigraphic and radiographic findings in the eight patients investigated are presented in Table I. In each patient there was exact correlation between scintigraphy with labelled red blood cells and the combination of radiocolloid scintigraphy, abdominal ultrasound, body computed tomography and chest radiography. The blood-pool images of two patients with involvement of several organs are shown in Figs. 2 and 3.

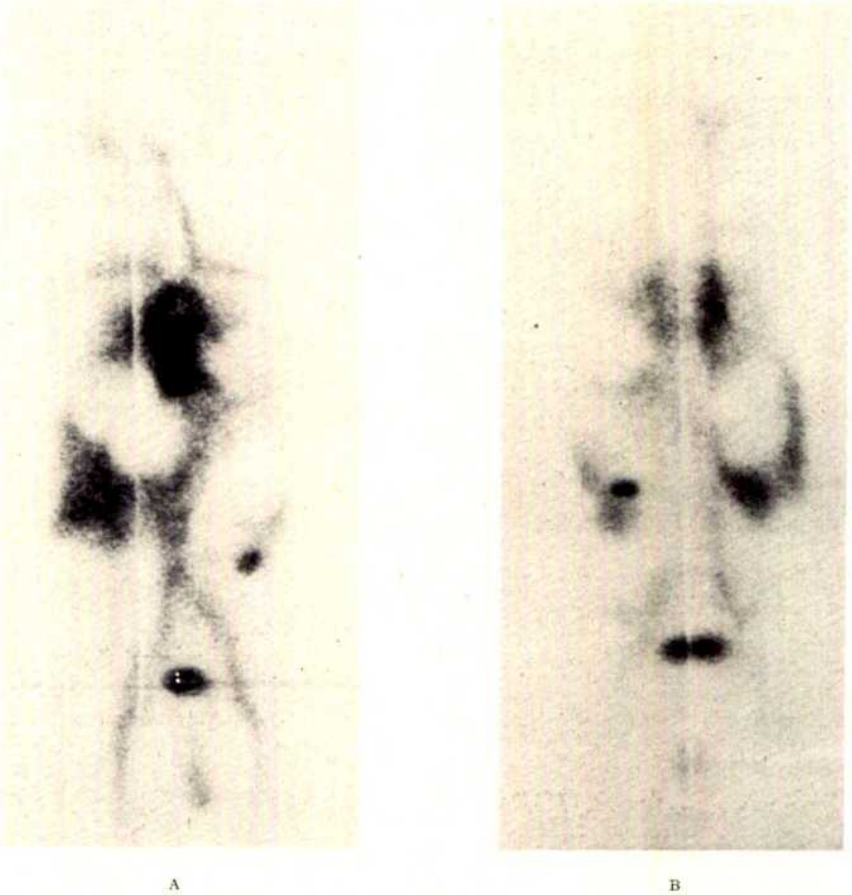


FIG. 3.

Whole-body scintigraphy with ^{99}Tc^m-labelled red blood cells in Case 2 (Table I) (A) Anterior view. (B) Posterior view. Cysts in liver and lung are demonstrated.

DISCUSSION

Cysts of *Echinoccocus granulosus* usually localize in the liver (55 to 75%) or in the lungs (15 to 25%). Both liver and lungs are infested in up to 25% of the cases. Other organs of possible involvement are spleen, kidneys, brain, pelvic organs, bones and muscles. Hydatid cysts cause symptoms by expansion and rupture (Reeder, 1970; Brown, 1975).

Patients can be evaluated by a combination of imaging modalities, each having its limitations. At present these techniques include radiocolloid liver scans, abdominal ultrasound, chest radiography and body computed tomography.

Radiocolloid liver scintigraphy can identify focal liver abnormalities, but it does not indicate the avascular nature of the lesion (Freeman and Johnson, 1975). Abdominal ultrasound is used to establish the cystic nature of the defects seen on prior radiocolloid liver scan, although in some institutions it is used for initial screening of the liver.

Diagnosis by chest radiography of involvement by echinoccocosis can be uncertain, as hydatid disease can imitate other diseases (Sutton, 1975). When the cyst matures it can lose its fibrous pericystic membrane and thus not maintain a sharp contour. It can then be difficult to differentiate by chest radiography from other circumscribed pulmonary lesions (Sutton, 1975).

The role of computed tomography in the evaluation of echinoccocosis has not yet been established. While probably of value in elucidating fine anatomical detail, it may not gain wide acceptance as a screening technique. Its high cost will probably prohibit widespread use in many countries where echinoccocosis is endemic; furthermore, the integral dose or mean dose received by the body is comparatively high when many sections are taken by CT scanning.

Whole-body blood-pool imaging is a simple, safe and inexpensive method which is suitable for screening of patients with hydatid disease.

A good correlation was found in the present study between scintigraphy with ^{99}Tc^{m}-labelled red blood cells and other imaging techniques (Table I). Although the case material presented is limited and additional studies are necessary to determine the sensitivity of the method, whole-body blood-pool imaging appears suitable for screening of patients with hydatid disease where involvement of several organs often occurs.

REFERENCES

BROWN, H. W. (Ed), 1975. *Basic Clinical Parasitology*, (Appleton-Century-Crofts, New York), pp. 120–135.

FREEMAN, L. and JOHNSON, P. (Eds), 1975. *Clinical scintillation imaging*. (Grune & Stratton, New York), pp. 425–430.

REEDER, M. M., 1970. Hydatid cyst of the lung (RPC of the month) *Radiology, 95*, 429–437.

RYO, Y., LEE, J. and HILARY, Z., 1974. Radionuclide angiography with Tc^{99}-labelled red blood cells for detection of aortic aneurysm. *Journal of Nuclear Medicine, 15*, 1014–1017.

SUTTON, D. (Ed), 1975. *A Textbook of Radiology* (Churchill Livingstone, London/N.Y.), pp. 305–315.

Book review

Practical Gastrointestinal Endoscopy. By P. B. Cotton and C. B. Williams. pp. ix+184, 1980 (Blackwell Scientific Publications, Oxford), £13·50.
ISBN 0-632-00274-3.

Doctors Cotton and Williams, two of the foremost British experts on endoscopy have combined to write a short manual on endoscopic techniques. The book covers all aspects of the procedures, including the modern sophisticated therapeutic advances, care of the equipment, role of the endoscopy nurse and documentation of findings, clearly and concisely. The book is lavishly illustrated, with clear diagrams, as well as having a useful list of instrument suppliers and basic references.

There is no other small handbook covering the field and the price is reasonable. This reviewer feels that the publication is of sufficient value to make it a required purchase for all endoscopy units that are concerned about the maintenance of high standards of endoscopy and who have any responsibility for the training of nurses and junior staff.

J. LEVI.

1981, *British Journal of Radiology*, *54*, 245–249 MARCH 1981

Effect of hyperthermia on the hypoxic fraction in an experimental mammary carcinoma *in vivo*

By Jens Overgaard, M.D.

The Institute of Cancer Research, Radiumstationen, DK-8000 Aarhus C, Denmark

ABSTRACT

The influence of hyperthermia on the fraction of clonogenic hypoxic cells in a C_3H mammary carcinoma was investigated using the TCD50 values for radiation treatment under normal or clamped conditions. A one-hour heat treatment at 41.5, 42.5 and 43.5°C given four hours after radiation reduced the hypoxic fraction to 2.3×10^{-1}, 7.4×10^{-3} and 6.5×10^{-3} respectively, when compared with the content of hypoxic cells in non-heated tumours. The results indicate that moderate hyperthermia is able to destroy selectively a large proportion of the fraction of radioresistant hypoxic cells in a solid tumour. This effect is probably due to the increased heat sensitivity of cells in a chronically hypoxic and nutritionally deprived acidic environment.

In the discussion about the rationale of combining hyperthermia with radiation in order to improve the radiation response of solid tumours, it has been suggested that heat may affect hypoxic cells more than cells in an oxygenated environment (Overgaard, 1977; 1978; Overgaard and Nielsen, 1980). This is probably not a consequence of heat-induced radiosensitization of hypoxic cells since several studies, with a few exceptions (Kim *et al.*, 1975; Robinson *et al.*, 1974), have shown that radiation alone and radiation combined with heat yield almost the same OER (Field and Bleehen, 1979; Myers and Field, 1979; Overgaard, 1980b; Power and Harris, 1977; Suit and Gerweck, 1979). It is unlikely that hypoxia itself increases the direct cytotoxic effect of hyperthermia (Gerweck *et al.*, 1979; Nielsen, 1980; Overgaard and Nielsen, 1980). However, the physiological changes in tumour areas chronically deprived of oxygen may create an environment strongly enhancing the direct lethal effect of heat. This may be due first of all to increased acidity (Field and Bleehen, 1979; Overgaard, 1977; 1978; Overgaard and Nielsen, 1980; Suit and Gerweck, 1979). Hill and Denekamp (1978) demonstrated that prolonged clamping of tumours drastically increased the sensitivity to hyperthermia, whereas a short clamping period, sufficient to produce radiobiological hypoxia, did not. Also histopathological studies have shown that moderate heat treatment selectively destroys cells in less vascularized areas of solid tumours (Overgaard, 1978; 1980b; Overgaard and Nielsen, 1980).

Furthermore, recent data have demonstrated that sequential treatment, where heat is given at least three to four hours after radiation, selectively increases the radiation response of solid tumours without causing any thermal enhancement in normal tissue (Gilette and Ensley, 1979; Hill and Denekamp, 1979; Overgaard, 1979; 1980b; Stewart and Denekamp, 1978). These findings can be interpreted as a selective destruction by heat of a radioresistant subpopulation of clonogenic tumour cells (Overgaard, 1980b).

The present experiments were performed to estimate the magnitude of a possible hyperthermic reduction of the hypoxic fraction in a solid experimental tumour.

MATERIALS AND METHODS

The tumour system has previously been described in detail (Overgaard, 1980a; 1980b). In brief, a C_3H mammary carcinoma transplanted to the feet of C3D2F1/Bom mice was treated at a size of 200 mm^3. Hyperthermia was applied by immersing the tumour-bearing leg into a water bath heated to 0.2°C above the required tumour temperature. Radiation was given with 250 kV X rays (15 mA, 1.1 mm Cu HVL, 1.9 Gy per minute). All animals were treated without anaesthetic. Hypoxia was produced by clamping the leg above the tumour with a rubber tube. Tumours irradiated in hypoxic conditions were clamped approximately eight minutes before and during the treatment in order to ensure full hypoxia.

As previous experiments have shown that heat applied to tumours four hours after irradiation causes no direct interaction between radiation and hyperthermia (Overgaard, 1980b), this procedure has been used in the present experiment. Tumours were irradiated either in air or under clamped conditions, and four hours later given a one-hour hyperthermic treatment.

The radiation doses needed to achieve on average 50% tumour control (TCD50) or complete moist desquamation on the tumour-bearing foot (DD50) were calculated by the logit method (Suit *et al.*,

---

Supported by the Danish Cancer Society (grant No. 24/79) and Krista and Viggo Petersen's Foundation.

1965). The hypoxic fraction was calculated on the basis of the vertical displacement of the dose-response curves according to the following equation (Howes, 1969):

$$\text{Hypoxic fraction} = \exp-((\text{TCD50 clamped}-\text{TCD50 air})/D_0\ \text{hypoxia}) \quad . \quad . \quad . \quad . \quad (1)$$

using a D_0 value of 3.2 Gy for hypoxic cells (Suit *et al.*, 1965).

The absolute number of tumour cells was estimated from the formula (Suit *et al.*, 1965):

$$\ln N = \text{TCD50 clamped}/D_0\ \text{hypoxia} - \ln n + \ln 0.693 \quad . \quad . \quad . \quad . \quad (2)$$

where N is the number of tumour cells, $D_0 = 3.2$ Gy and the extrapolation number $n = 3$.

RESULTS

Table I shows the effect on the hypoxic fraction of heating for one hour at various temperatures. Experiments with radiation under normal or clamped conditions indicate that this mammary carcinoma contains approximately 8% of hypoxic clonogenic cells. A one-hour heat treatment at 41.5°C reduced this fraction to just below 2%. However, a further increase of the temperature to 42.5 or 43.5°C (all measured as tumour temperature) caused a dramatic decrease of the hypoxic fraction, by a factor of more than 100. This was almost the same after heating at 42.5 or 43.5°C.

The one-hour heating at 43.5°C also apparently caused some reduction in the number of oxygenated cells, since the clamped TCD50 was reduced to 50.8 Gy compared with 64.5 Gy observed after radiation alone. This is seen in Fig. 1 which shows that hyperthermic treatment at 43.5°C for one hour significantly reduces the absolute number of both total and hypoxic clonogenic cells in the tumour. In fact, this treatment reduces the absolute number of hypoxic cells from approximately 2.1×10^7 in the non-heated tumours to about 2000.

It was not clear if clamping itself might have altered the subsequent sensitivity to hyperthermia. This was investigated by clamping the tumours for 30 minutes before irradiation in air, followed after four hours by hyperthermia. Table II shows that this procedure, when compared with the values

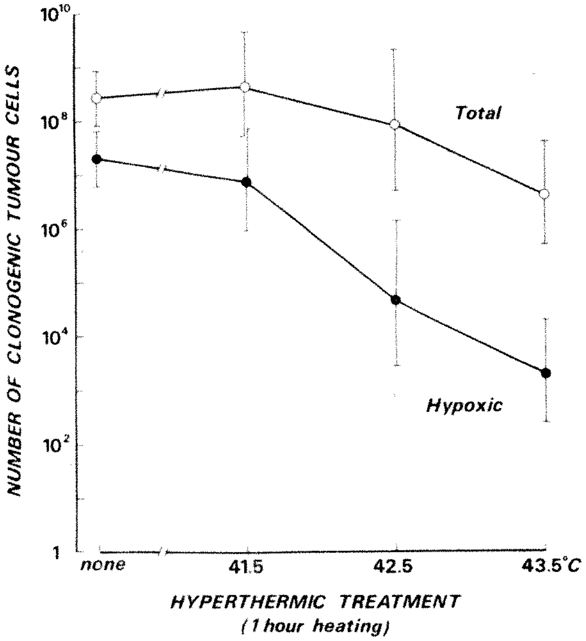


FIG. 1.

Estimated values of absolute number of clonogenic tumour cells (open circles) following different heat treatments. The closed circles represent the absolute number of hypoxic cells obtained by multiplying the total number of cells by the hypoxic fraction (Table I). The vertical bars indicate 95% confidence limits obtained from corresponding errors in the TCD50 values.

TABLE I

EFFECT OF HYPERTHERMIA ON THE HYPOXIC FRACTION OF CLONOGENIC TUMOUR CELLS IN A C_3H MAMMARY CARCINOMA

Heat treatment*	TCD50 air (Gy)	TCD50 hypoxia (Gy)	Hypoxic fraction	Relative proportion of hypoxic cells§
None (radiation alone)†	56.3 (54.9–57.8)‡	64.5 (60.7–68.5)	7.7×10^{-2}	1.0
41.5°C/60 min	53.1 (48.9–57.7)	66.0 (59.3–73.4)	1.8×10^{-2}	2.3×10^{-1}
42.5°C/60 min	36.9 (28.9–47.1)	60.8 (51.7–71.5)	5.7×10^{-4}	7.4×10^{-3}
43.5°C/60 min	26.7 (23.2–30.7)	51.0 (44.4–58.5)	5.0×10^{-4}	6.5×10^{-3}

*Given four hours after radiation.

†Given at room temperature.

‡Numbers in brackets represent 95% confidence limits.

§$\dfrac{\text{Hypoxic fraction (radiation + heat)}}{\text{Hypoxic fraction (radiation alone)}}$

obtained from tumours treated without pre-clamping, did not significantly change the TCD50. The skin showed moist desquamation DD50 values of 26.5 and 65.5 Gy with radiation treatment alone given in air or hypoxia respectively. These values give an OER of 2.46 for the skin covering the tumour, showing that clamping caused radiobiological hypoxia.

DISCUSSION

This study demonstrates that a moderate heat treatment, which does not enhance the radiation response in normal tissue, reduced the hypoxic fraction in a solid tumour by a factor of more than 100 and the absolute number of hypoxic clonogenic cells to about 2×10^{-5} of the original content. Although it was not demonstrated in the present study, it is probable that this effect is primarily caused by a hyperthermic destruction of the nutritionally deprived, chronically hypoxic tumour-cell population. A similar conclusion was reached by Dewey *et al.* (1977) by analysing survival curves constructed from TCD50 experiments in a C_3H mammary carcinoma treated with combined heat and radiation. Cells which are acutely hypoxic due to vascular fluctuations (Brown, 1979), but otherwise situated in a normal physiological environment, may not be affected to the same extent.

A number of factors related to the experimental design and the theoretical calculations may influence the results and conclusions of the present study.

First, it has to be shown that the clamping procedure will not influence the effect of the subsequent heat treatment, since even small changes in the tumour physiology may alter the heat sensitivity. However, when the tumour was clamped for 30 minutes before any other treatment was given, this did not induce changes significantly influencing the tumour response to either radiation or hyperthermia given in the present treatment schedules (Table II).

The four-hour interval between radiation and heat was chosen because previous studies (Overgaard, 1979; 1980a; 1980b) have shown that heat treatment given with this sequence and interval in relation to radiation seems not to result in any direct hyperthermic radiosensitization. This is seen in Fig. 2 which shows that the thermal enhancement of radiation damage in the skin gradually decreases with increasing interval between radiation and heat and with intervals of four hours or longer no thermal enhancement can be detected. Similarly, the thermal enhancement ratio (TER) for the tumour response gradually decreases with increasing interval between radiation and hyperthermia. However, the tumour TER reaches a plateau value of approximately 1.5

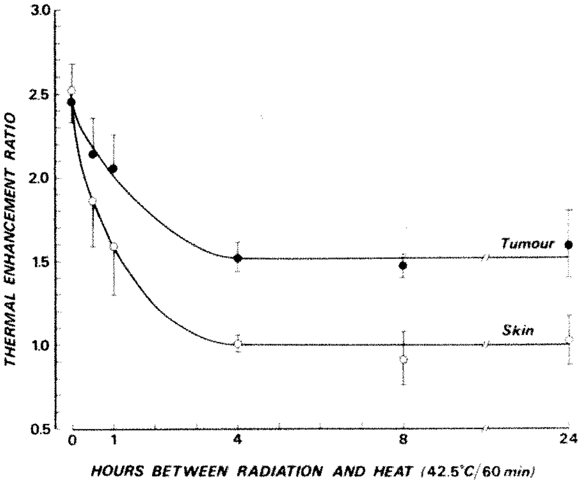


FIG. 2.

Thermal enhancement ratio (TER) as a function of interval between radiation and heat treatment. Both tumour and surrounding skin show a gradual decrease with intervals up to four hours, after which a plateau is obtained. This may indicate absence of hyperthermic radiosensitization with intervals of four hours and over. Vertical bars represent 95% confidence limits.

$$\mathrm{TER}: \frac{\text{response dose of radiation}}{\text{response dose of radiation with heat}}.$$

TABLE II

EFFECT OF CLAMPING BEFORE IRRADIATION OF A C_3H MAMMARY CARCINOMA

Heat treatment*	Radiation in air without pre-clamping TCD50 (Gy)	30 min clamping before irradiation in air TCD50 (Gy)	$\frac{\text{TCD50 air (no clamping)}}{\text{TCD50 air (pre-clamping)}}$
None (radiation alone in room temperature)	56.3 (54.9 – 57.8)†	56.9 (53.6 – 60.4)	0.99 (0.90 – 1.09)
42.5°C/60 min	36.9 (34.6 – 39.4)	40.2 (34.6 – 46.9)	0.92 (0.86 – 0.98)
43.5°C/60 min	26.7 (23.2 – 30.7)	26.4 (23.7 – 29.3)	1.01 (0.79 – 1.28)

*Given four hours after radiation.
†Numbers in brackets represent 95% confidence limits.

for intervals of four hours or more (Fig. 2). In view of the observations made in normal tissues and cell cultures (Field and Bleehen, 1979; Overgaard, 1981b) this elevated TER is not likely to be due to a persistent thermal radiosensitization in the tumour, but may reflect a hyperthermic destruction of radioresistant chronically hypoxic tumour cells (Overgaard, 1980b; 1981b). Thus, it is unlikely that any direct hyperthermic radiosensitization will occur with the sequential treatment schedule applied in the present experiments.

The assumed value of D_0 is critical for the quantitative results obtained from the theoretical calculation. In the present tumour, a D_0 value of 3.2 Gy for hypoxic tumour cells was judged to be most appropriate, based primarily on the work by Suit *et al.* (1965). A different D_0 value will tend to alter the estimation of the hypoxic fraction and the absolute number of clonogenic tumour cells. However, this will not cause any major changes in the relative differences observed after the various treatment regimes, and will therefore not significantly influence the conclusions of the present study.

Also the formula (2) used for estimation of the total cell number contains a number of assumptions. This includes, besides D_0, the extrapolation number n for which a value of three was chosen, again based on the work by Suit *et al.* (1965). The reader is referred to this paper for more detailed discussions of the problems. That the assumption seems reasonable can be seen from the estimated total cell number, which in a non-heated tumour with a size of 200 mm^3 was found to be approximately 2×10^8.

The present results support the assumption that the increased radiation response of tumours that have been treated sequentially with radiation and hyperthermia is mainly caused by a selective hyperthermic destruction of a proportion of the radioresistant hypoxic tumour cells. However, not all the hypoxic cells are destroyed. Recent experiments (Overgaard, 1980a) indicate that additional treatment with the hypoxic radiosensitizer, misonidazole, may cause a further increase in the response of the tumour to radiation; after such treatment the therapeutic gain was almost trebled. It may be argued that the additional effect of misonidazole is due to radiosensitization of tumour cells which are acutely hypoxic, but otherwise situated in a more normal physiological environment, and thereby less heat sensitive than the chronically hypoxic population.

Currently, many attempts are made to employ hyperthermia as an adjuvant to radiotherapy in clinical practice. The optimal treatment schedules for such combined heat and radiation may depend on the ability to achieve a selective local tumour heating without heating the surrounding normal tissue (Overgaard, 1979; 1981a; 1981b). The fact that our findings show that heat itself is able to destroy selectively a large proportion of radioresistant tumour cells makes it reasonable to suggest that a sequential schedule should form the basis for clinical application of the combined treatment since it is questionable if such treatment causes any additional damage to the normal tissue (Field and Bleehen, 1979; Hill and Denekamp, 1979; Overgaard, 1979; 1981a; 1981b; Stewart and Denekamp, 1978).

REFERENCES

BROWN, J. M., 1979. Evidence for acutely hypoxic cells in mouse tumours, and a possible mechanism of reoxygenation. *British Journal of Radiology*, *52*, 650–656.

DEWEY, W. C., THRALL, D. E. and GILLETTE, E. L., 1977. Hyperthermia and radiation—a selective thermal effect on chronically hypoxic tumor cells *in vivo*. *International Journal of Radiation Oncology, Biology, Physics*, *2*, 99–103.

FIELD, S. B. and BLEEHEN, N. M., 1979. Hyperthermia in the treatment of cancer. *Cancer Treatment Reviews*, *6*, 63–94.

GERWECK, L. E., NYGAARD, T. G. and BURLETT, M., 1979. Response of cells to hyperthermia under acute and chronic hypoxic conditions. *Cancer Research*, *39*, 966–972.

GILLETTE, E. L. and ENSLEY, B. A., 1979. Effect of heating order on radiation response of mouse tumor and skin. *International Journal of Radiation Oncology, Biology, Physics*, *5*, 209–213.

HILL, S. A. and DENEKAMP, J., 1978. The effect of vascular occlusion on the thermal sensitization of a mouse tumour. *British Journal of Radiology*, *51*, 997–1002.

1979. The response of six mouse tumours to combined heat and X rays: implications for therapy. *British Journal of Radiology*, *52*, 209–218.

HOWES, A. E., 1969. An estimation of changes in the proportions and absolute numbers of hypoxic cells after irradiation of transplanted C$_3$H mouse mammary tumours. *British Journal of Radiology*, *42*, 441–447.

KIM, S. H., KIM, J. H. and HAHN, E. W., 1975. The radiosensitization of hypoxic tumor cells by hyperthermia. *Radiology*, *114*, 727–728.

MYERS, R. and FIELD, S. B., 1979. Hyperthermia and the oxygen enhancement ratio for damage to baby rat cartilage. *British Journal of Radiology*, *52*, 415–416.

NIELSEN, O. S., 1980. Effect of fractionated hyperthermia on hypoxic cells *in vitro*. *International Journal of Radiation Biology and Related Studies in Physics, Chemistry and Medicine* (in press).

OVERGAARD, J., 1977. Effect of hyperthermia on malignant cells *in vivo*. A review and a hypothesis. *Cancer*, *39*, 2637–2646.

1978. The effect of local hyperthermia alone and in combination with radiation, on solid tumors. In *Cancer Therapy by Hyperthermia and Radiation. Proceedings of the 2nd International Symposium, Essen, June 2–4, 1977*, Eds. C. Streffer *et al.* (Urban and Schwarzenberg, Baltimore and Munich), pp. 49–61.

1979. Hyperthermia and radiotherapy. In *Advances in Medical Oncology, Research and Education*, Ed. M. Moore, Vol. 6 (Pergamon Press, Oxford and New York), pp. 235–245.

1980a. Effect of misonidazole and hyperthermia on the radiosensitivity of a C$_3$H mouse mammary carcinoma and its surrounding normal tissue. *British Journal of Cancer*, *41*, 10–21.

1980b. Simultaneous and sequential hyperthermia and radiation treatment of an experimental tumor and its surrounding normal tissue *in vivo*. *International Journal of Radiation Oncology, Biology, Physics*, *6*, 1507–1517.

1981a. Fractionated radiation and hyperthermia. Experimental and clinical studies. *Cancer* (in press).

1981b. Influence of sequence and interval on the biological response to combined hyperthermia and radiation. *Journal of the National Cancer Institute Monograph* (in press).

OVERGAARD, J. and NIELSEN, O. S., 1980. The role of tissue environmental factors on the kinetics and morphology of tumor cells exposed to hyperthermia. *Annals of the New York Academy of Sciences*, *335*, 254–278.

POWER, J. A. and HARRIS, J. W., 1977. Response of extremely hypoxic cells to hyperthermia: survival and oxygen enhancement ratios. *Radiology*, *123*, 767–770.

ROBINSON, J. E., WIZENBERG, M. J. and MCCREADY, W. A., 1974. Combined hyperthermia and radiation suggest an alternative to heavy particle therapy for reduced oxygen enhancement ratios. *Nature*, *251*, 521–522.

STEWART, F. A. and DENEKAMP, J., 1978. The therapeutic advantage of combined heat and X rays on a mouse fibrosarcoma. *British Journal of Radiology*, *51*, 307–316.

SUIT, H. and GERWECK, L. E., 1979. Potential for hyperthermia and radiation therapy. *Cancer Research*, *39*, 2290–2298.

SUIT, H. D., SHALEK, R. J. and WETTE, R., 1965. Radiation response of C3H mouse mammary carcinoma evaluated in terms of cellular radiation sensitivity. In *Cellular Radiation Biology* (Williams and Wilkins, Baltimore) pp. 514–530.

Book reviews

Nuclear Medicine Annual 1980. Ed. Leonard M. Freeman, pp. xi + 440 (Raven Press, New York), $53.72.
ISBN 0-89004-472-4

One of the problems in nuclear medicine is to keep abreast of the rapidly changing field. It is one of those disciplines where experimental work is transformed into a practical routine test in a matter of months. For some time Freeman has edited the extremely successful "Seminars in Nuclear Medicine" which has provided a useful means of updating one's knowledge. Now from the same editor comes a hardback annual planned to appear each year to coincide with the annual meeting of the Society of Nuclear Medicine. Each edition is destined to have ten in-depth reviews of mainly clinical subjects but with some articles devoted to basic sciences. The aim is to keep the reviews up to date by rapid publication.

The first volume in the series contains articles on thallium 201 imaging, pulmonary nuclear medicine, emission tomography, adrenal scanning, benign radionuclide imaging and quantitative renal-function scanning. There is also an update on detection of venous thrombosis and the comparison of CT scanning, ultrasound and nuclear imaging. The authors are all recognized authorities in their fields. The standard of the articles is uniformly good, they cover the subjects fully with an adequate number of well reproduced illustrations, and are fully referenced.

This book is a welcome addition to the nuclear medicine literature and will be especially valuable as a quick means of keeping abreast of the latest developments for those who have limited time to wade through the increasing numbers of articles and journals devoted to imaging topics.

V. R. MCCREADY.

1980 Year Book of Nuclear Medicine. Ed. by James L. Quinn, III, pp. 335, 1980. (Year Book Medical Publishers, Inc., Chicago/London), £25·50.
ISBN 0-8151-6989-2

This is the 15th volume in the series. It follows the pattern of its predecessors in presenting extended summaries, with one or two illustrations or tables, of a couple of hundred selected papers which appeared during the year. Most of the papers are clinical, grouped under the various body systems, with the heart and great vessels and gastrointestinal system taking the largest share, reflecting their current position as the main growth areas in nuclear medicine. The many readers who are familiar with previous volumes can continue to look for the Editor's pithy one-line comment at the end of each item before deciding to read it in full.

The early volumes in the series could be criticized for an undue emphasis on papers published in specialist nuclear medicine journals and then only those published in the USA. This no longer applies, and relevant papers from journals dealing with many other specialties such as cardiology and endocrinology are covered, thus increasing the value of this book to the nuclear medicine specialist.

With hindsight, the personal statement by the Editor which forms the short introduction takes on a deeper significance following the recent announcement of his untimely death. With this last volume he has set a high standard for his successors.

N. VEALL.

1981, *British Journal of Radiology*, *54*, 250–254

Effect of X irradiation on the rectum of the rat

By *F.-H. Hubmann

Institut für Biologie, Gesellschaft für Strahlen- und Umweltforschung (GSF), Ingolstädter Landstrasse 1, D-8042-Neuherberg-München, Federal Republic of Germany

(*Received April 1980 and in revised form August 1980*)

ABSTRACT

It is demonstrated how a definite part of the rectum of the female Wistar rat can be selectively irradiated without surgery. The effect of X irradiation on the rectum is in the acute phase (second week after irradiation) a haemorrhagic radiation proctitis and in the chronic phase a rectal obstruction. The dose-effect relationship using rectal obstruction as the end point is a sigmoid curve with a ED_{10} of 17.50 Gy, ED_{50} of 21.5 Gy and ED_{90} of 27.5 Gy. Latency time decreases exponentially with increasing dose and is 150 days at the ED_{50}. Histological findings show mucosal glands and cysts within the submucosa and a severe submucosal radiation fibrosis which results in the rectum becoming a rigid and non-elastic tube which leads to a functional block in transport of faeces.

The radiotherapist's task would be an easy one if the only consideration was to give a large enough dose to a tumour to sterilize it. The limitation has always been the amount of damage which can be tolerated by normal tissues lying within the radiation field. The study of normal tissue damage and its underlying cause must therefore form a large part of radiobiological research. The intestine is always a dose-limiting tissue when it lies in the radiation field. It is therefore of importance to study the radiosensitivity of this tissue in order to predict the radiation conditions under which the least damage may be inflicted (Hornsey, 1973).

Evidence of injury to the intestinal tract by irradiation was first reported by Walsh in 1897, but the first fatal case with autopsy findings was not published until 1917 (Franz and Orth, 1917). Since then a large number of cases have been reported. Usually the damage (ulceration, perforation, formation of fistula, adhesion, stricture) followed irradiation of carcinoma of the uterus, but it has occasionally arisen during treatment of other intra-abdominal structures, *e.g.* bladder and ovary (Mulligan, 1942; Chau *et al.*, 1962; Dean and Taylor, 1960; Gray and Kottmeier, 1957; Ingelman-Sundberg, 1947; Kaplan *et al.*, 1965; Strickland, 1954; Strickland and Gregory, 1961; Todd, 1938; Twombly *et al.*, 1952; Colcock and Hume, 1959). The incidence of rectal damage appears to vary from 2 to 5% according to various authors (Wigby, 1943; Maas, 1948; Perkins and Spjut, 1962; Russel and Welch, 1979).

Very little work has been reported to determine how much irradiation the rectum can actually tolerate without permanent injury. It is the purpose of this paper to attempt to define the limits of tolerance of the rectum to irradiation.

METHODS

Adult female Wistar rats weighing 230–280 g were used in this study. They were kept individually in trellis cages in which the excreta could be collected quantitatively. Food and water were given *ad libitum*.

Food was removed one day before irradiation but water was available *ad libitum*. Also one day before irradiation, whilst the rats were anaesthetized with ether, 1 ml of the laxative Microklist* (Pharmacia AS, Hilleröd, Denmark) was injected into the large intestine by means of a syringe, the tip of which was tapered approximately to the diameter of the anus. Defaecation started 10 minutes after injection. The procedure was repeated three hours later; one day after purging, the intestine was almost empty.

For irradiation the rats were anaesthetized by intraperitoneal injection of sodium pentobarbitone (4.5 mg/100 g).

An empty urinary bladder is necessary for this radiation technique to ensure that this organ lies outside the radiation field. Therefore a thin plastic catheter (external diameter 1 mm, internal diameter 0.5 mm) was placed carefully into the urethra and moved forward into the bladder so that urine was delivered when the abdomen was pressed.

A steel nail (5 × 0.3 cm) coated with paraffin was dipped into glycerine and pushed gently forward into the empty rectum until the head of the nail reached the anus. This caused no injury as the rectum of the female Wistar rat is straight and the size of the nail was adapted to the rectum.

The rat was taped by the tail so that it hung head down in a vertical position with its back on a lead wall (24.5 × 37 × 0.3 cm) containing a window (1 × 2.2 cm). In this position the other abdominal organs fell away from the irradiation field. A radiograph of the position of the rectum containing the nail within the window of the lead wall was taken.

---

*Present address: Neurologische Klinik, D-7959-Schwendi-Dietenbronn, Federal Republic of Germany.

The tube of the Picker-Mueller-MG 300 X-irradiation unit (C. H. F. Mueller GmbH, Hamburg) was shifted horizontally and a holder (Polaroid land film holder 500) with a polaroid film (Polaroid 4×5, land film type 51; Polaroid Corp., Cambridge, Mass.) was placed behind the rat. Conditions for taking the radiograph were: focus-film distance 34 cm, 1 mA, 100 kV, 0.6 mm Cu+1 mm Al filter, 10 s, giving a dose of about 1 cGy (rad) to the rectum. The position of the rectum was correct if the nail appeared in the middle of the window and its tip reached the lower margin. This position allowed selective irradiation of a definite part of the rectum *in situ* without the urethra, bladder, ureters, kidneys, liver, spleen, small intestine or spinal cord receiving any radiation. The nail was carefully removed by slowly drawing it out along the mid-line after taking the radiograph.

The rectum was then irradiated *in situ* at 22 cm FSD with X rays (9 mA, 300 kV, 0.6 mm Cu+1 mm Al). Various times of irradiation were used to give doses ranging from 15 Gy to 30 Gy (1500–3000 rad). A single treatment was given using one field. The absorbed X-ray dose in the rectum was measured with TLD using lithium fluoride rods (1×1×6 mm; Harshaw Chemie GmbH, Wermelskirchen, Germany). *In vivo* dosimetry showed that the dose rate in the rectum was 1.9 Gy /min.

Frequency and consistency of defaecation and blood in faeces were examined every second day by means of the benzidine reaction (Merck, 1970). Rats which died were autopsied and a light microscopic study of the irradiated rectum performed using azan staining (Romeis, 1968) and resorcinol fuchsin staining (Romeis, 1968).

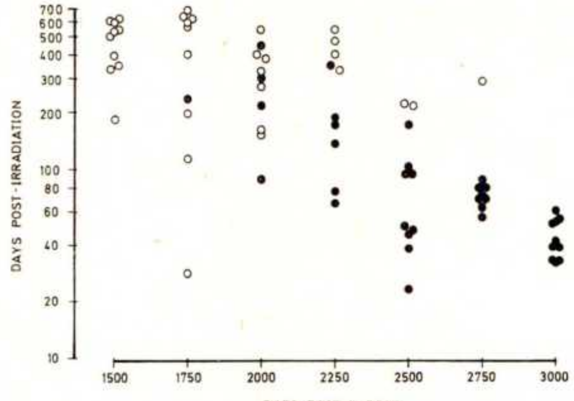


FIG. 1.

Relationship between dose, duration of life after irradiation and occurrence of obstruction of the rectum. (○) Died without rectal obstruction; (●) died with rectal obstruction.

RESULTS

The irradiation was apparently well tolerated by the rat with mild skin reactions. In addition to loss of hair in the radiation field a superficial ulceration could be observed.

The consistency of the faeces in the irradiated rats was the same as in control animals. No diarrhoea occurred and no excess secretion of mucin in stools was observed. However, between the seventh and sixteenth day after irradiation a haemorrhagic radiation proctitis occurred; on examination of the stools slight bleeding from the injured mucosa was observed. The acute radiation proctitis tended to subside without treatment. In contrast, the late reactions were fibrosis and rectal stricture which led to luminal obstruction and death.

From the autopsy findings the irradiated animals can be divided into those with and without rectal obstruction. After various times, rats with rectal obstruction showed a progressing enlargement of the abdomen and cessation of defaecation (Fig. 1). Seven to nine days after the onset of these symptoms the animals died. At autopsy the irradiated part of the rectum showed a dark colour, felt hard and was obstructed; proximal to the irradiated part the

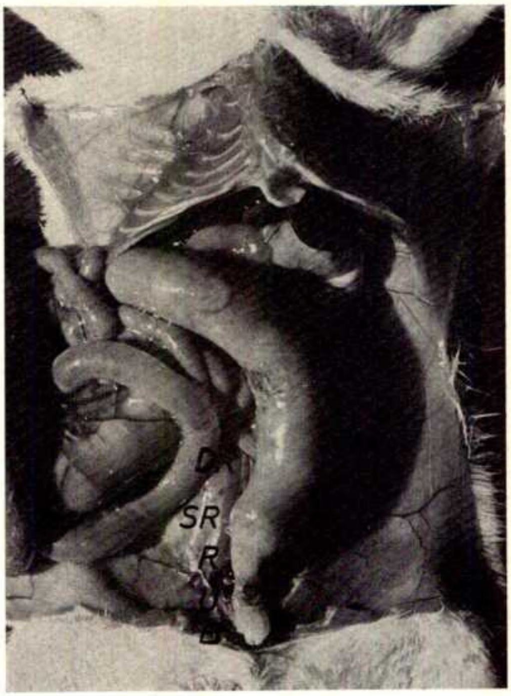


FIG. 2.

Autopsy finding: rectal obstruction. Note urinary bladder (B), uterus cut off (U), rectum (R), stenotic portion of rectum (SR), dilated rectum (DR).

TABLE I

Experimental results

Dose (Gy) in the rectum	Number of animals	Rectal obstruction (%)	Number of hydroureters with hydronephroses	Number of obliterated ureters
15	10	0	0	0
17.5	10	10	2	2
20	11	36	1	0
22.5	10	60	1	0
25	11	82	2	1
27.5	10	90	2	0
30	10	100	1	1

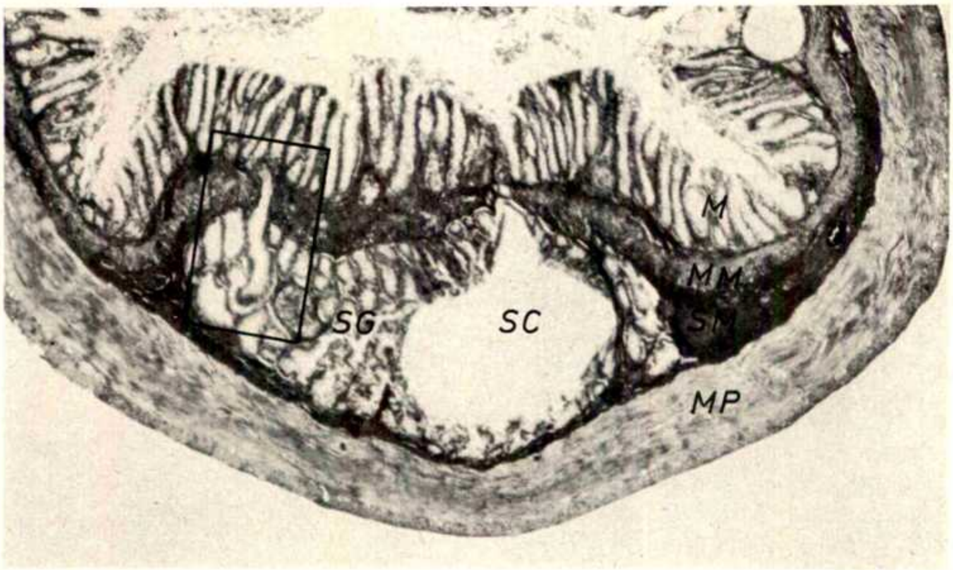


Fig. 3.

Histology of rectum 150 days after irradiation with 25 Gy (azan, × 50). Note submucosal mucinous glands (SG) and cyst (SC), mucosa (M), muscularis mucosae (MM), submucosa (SM), muscularis propria (MP). The area outlined by the rectangle is enlarged in Fig.5.

rectum was extremely dilated and filled with faeces whereas the distal part was empty (Fig. 2). In some animals hydroureter and hydronephrosis could be observed. Injection of ink into the lumen of the ureter, however, showed that obstruction was permanent in only a few cases (Table I).

Rats without rectal obstruction died after various times showing almost no pathological findings at autopsy. In the radiation field the rectum was dark and hard but no stenotic portion was seen.

No induction of colonic neoplasms by X irradiation was observed. The colon did not adhere to the surroundings and the rectum did not become fixed as in a so-called "frozen pelvis".

The results are listed in Table I and Fig. 1. The end point of the investigation is rectal obstruction. The experimental data of Table I can be represented as a sigmoid curve giving ED_{10} of 17.5 Gy, ED_{90} of 27.5 Gy, and ED_{50} 21.5 Gy. The latency time for rectal obstruction decreases exponentially with increasing dose. At 21.5 Gy ED_{50} latency time is 150 days.

The specimen removed at autopsy consisted of a segment of the irradiated rectum. One strictured area was found. The serosa over the area was thickened, opaque and brownish. Upon opening the bowel, the stricture, measuring 1 cm in length, showed a very narrow lumen. The mucosa was atrophic and the wall was thickened by whitish hard tissue and seemed fibrotic. The lumen of the rectum proximal to the stricture was markedly distended and showed a flattened mucosa with thin walls, whereas distal to the stricture no pathological alterations were observed.

Figure 3 shows the histological findings in a rectum 150 days after irradiation to 25 Gy. Radiation

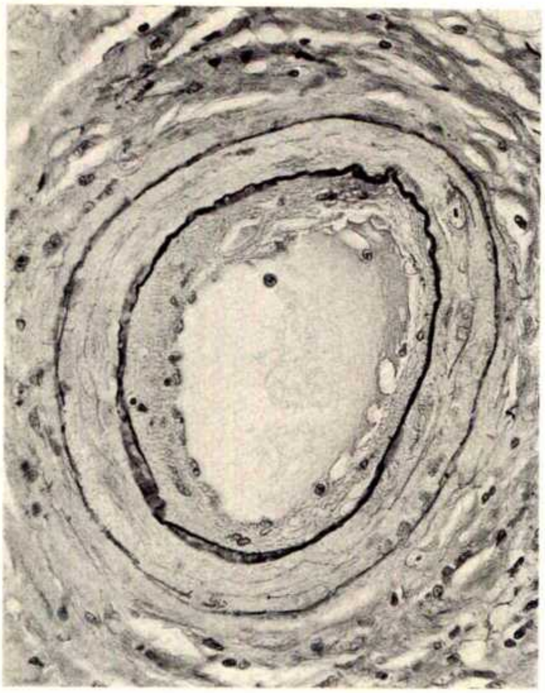


FIG. 4.

Small artery with narrow lumen; 50 days after irradiation with 22.5 Gy (resorcinol fuchsin, ×391).

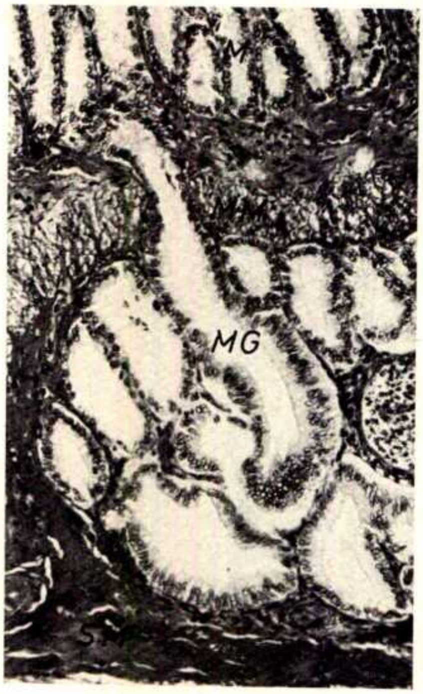


FIG. 5.

Detail of Fig. 3, showing rectal mucinous gland (MG) extending beyond the disrupted muscularis mucosae (MM); 150 days after irradiation with 25 Gy (azan, ×200). Note mucosa (M), submucosa (SM).

fibrosis in the submucosa was found to be accompanied by proctitis cystica profunda (Epstein *et al.*, 1966; Wayte and Helwig, 1967; Buckwalter and Kent, 1972) and the entire microscopic examination can be described as a radiation-induced proctitis fibrosa cystica profunda. The mucosa showed both atrophic and hyperplastic areas. The muscularis mucosae was fragmented and absent in many parts, giving the appearance of continuity between the mucosa and the submucosa which was extremely thickened by radiation fibrosis. The blood vessels were numerous and dilated. The small arteries showed proliferation of the endothelium, thickening and hyalinization of their walls, resulting in severe narrowing of the lumen (Fig. 4).

In many areas, the normal mucosal glands extended into and beyond the disrupted muscularis mucosae (Fig. 5) and formed numerous various-sized cysts in the submucosa (Fig. 3). Mucosal glands and cysts beneath the muscularis mucosae were found in 40% of the irradiated animals. Most of the cysts were lined with columnar, mucin-secreting epithelium, others by flattened cells, and some had no lining at all, so that pools of mucin appeared to lie free in the stroma. The epithelium lining some cysts showed prominent nuclei and there was no cytological evidence of malignancy. This histological picture was consistent with proctitis cystica profunda (Baratz *et al.*, 1978).

DISCUSSION

The human rectum is known to be a relatively radioresistant organ. The tolerance dose for the rectum is 55 Gy (5500 rad) of X rays in about 38 days, this dose causing severe complications in not more than 5% of cases within five years after treatment (Rubin and Casarett, 1972).

The early reactions (during the course of therapy for pelvic neoplasms) include hypermotility and tenesmus. This period corresponds to the oedematous, hyperemic mucosal changes throughout the rectum. Most patients experience relief from the symptoms upon cessation of therapy. Although the late reactions (where tolerance is exceeded) may occur within the first year after the completion of treatment, they more usually present insidiously one to two years later. They are much more serious than the early reactions. With the development of rectal and/or perirectal fibrosis and healing of the ulceration, a stenosing process can result (Rubin and

Casarett, 1968). The general prognosis is critical and the ultimate outcome rests on the severity of the stenosis, fistulization (mainly between rectum and vagina), ulceration, bleeding or pain.

In the present study, rectal obstruction after irradiation was considered to be a good indicator of radiation damage and has been used as an experimental model to measure the extent of radiation injury in rats.

The radiation procedure allowed selective irradiation to a certain part of the rectum *in situ* avoiding all surrounding organs. About seven days after irradiation a haemorrhagic radiation proctitis occurred leading to bloody faeces, but healed within a further nine days.

The histological findings of the late reaction showed a severe radiation fibrosis, mainly in the submucosa of the irradiated rectum, leading to loss of elasticity. The irradiated rectum was not closed, but the hard and non-elastic fibrosis formed a rigid tube which did not allow sufficient elasticity for the further transport of formed faeces. This functional block at the irradiated part of the rectum caused a proximal accumulation of faeces with an enormous dilatation of the large intestine whereas distal to the block the rectum was empty. Cessation of defaecation with progressive enlargement of the abdomen allowed the diagnosis of rectal obstruction to be made in each animal. The sigmoid dose-response curve using rectal obstruction as the end point is between 17.5 Gy (ED_{10}) and 27.5 Gy (ED_{90}) with a ED_{50} of 21.5 Gy.

During rectal obstruction the enormously dilated rectum sometimes caused compression of the ureters lying beside the colon. This resulted in hydroureter and hydronephrosis although the ureters were not closed by obliteration. However, several ureters were totally obstructed (Table I) possibly due to inaccurate handling of the irradiation set-up.

Whereas the death of animals without rectal obstruction was independent of dose, animals with rectal obstruction showed a dose-dependent duration of life. Increasing rectal dose resulted in exponentially decreasing latency time for rectal obstruction. Latency time after 30 Gy was only one-sixth of that after 20 Gy and was about 44 days.

REFERENCES

Baratz, M., Werbin, N., Wiznitzer, T. and Rozen, P., 1978. Irradiation-induced colonic stricture and colitis cystica profunda: report of a case. *Diseases of the Colon and Rectum*, *21*, 75–79.

Buckwalter, J. A. and Kent, T. H., 1972. Ectopic submucosal glands in the colon. *Archives of Pathology and Laboratory Medicine*, *93*, 562–564.

Chau, P. M., Fletcher, G. H., Rutledge, F. N. and Dodd, G. D., 1962. Complications in high dose whole pelvis irradiation in female pelvic cancer. *American Journal of Roentgenology*, *87*, 22–40.

Colcock, B. P. and Hume, A., 1959. Radiation injury to the sigmoid and rectum. *Surgery Gynecology and Obstetrics*, *109*, 306–312.

Dean, R. E. and Taylor, E. S., 1960. Surgical treatment of complications resulting from irradiation therapy of cervical cancer. *American Journal of Obstetrics and Gynecology*, *79*, 34–42.

Epstein, S. E., Ascari, W. Q., Ablow, R. C., Seaman, W. B. and Lattes, R., 1966. Colitis cystica profunda. *American Journal of Clinical Pathology*, *45*, 186–201.

Franz, K. and Orth, J., 1917. Fall einer Röntgenschädigung. *Berliner Klinische Wochenschrift*, *54*, 662–664.

Gray, M. J. and Kottmeier, H. L., 1957. Rectal and bladder injuries following radium therapy for carcinoma of the cervix at the Radiumhemmet. *American Journal of Obstetrics and Gynecology*, *74*, 1294–1303.

Hornsey, S., 1973. The radiosensitivity of the intestine. In *Strahlenschutz in Forschung und Praxis*, *vol. XIII*, pp. 78–88. (G. Thieme, Stuttgart).

Ingelman-Sundberg, A., 1947. Rectal injuries following radium treatment of cancer of the cervix uteri. *Acta Radiologica* (*Stockholm*), *64*, 1–79.

Kaplan, A. L., Hudgins, P. T. and Wall, J. A., 1965. Postradiation pelvic fibrosis simulating recurrent carcinoma. *American Journal of Obstetrics and Gynecology*, *92*, 117–124.

Maas, J. M., 1948. Intestinal changes secondary to irradiation of pelvic malignancies. *American Journal of Obstetrics and Gynecology*, *56*, 249.

Merck, E., 1970. *Klinisches Labor* (Merck, Darmstadt).

Mulligan, R. M., 1942. The lesions produced in the gastrointestinal tract by irradiation. *American Journal of Pathology*, *18*, 515–527.

Perkins, D. E. and Spjut, H. J., 1962. Intestinal stenosis following radiation therapy. *American Journal of Roentgenology*, *88*, 953–966.

Romeis, B., 1968. *Mikroskopische Technik* (Oldenbourg, München).

Rubin, P. and Casarett, G., 1968. Alimentary tract: small and large intestines and rectum. In *Clinical Radiation Pathology*, Vol. 1, pp. 193–240. (W. B. Saunders Company, Philadelphia).

1972. A direction for clinical radiation pathology: the tolerance dose. In *Frontiers Radiation Therapy Oncology*, Vol. 6, pp. 1–16. (University Park Press, Baltimore).

Russel, J. C. and Welch, J. P., 1979. Operative management of radiation injuries of the intestinal tract. *American Journal of Surgery*, *137*, 433–440.

Strickland, P., 1954. Damage to the rectum in the radium treatment of carcinoma of the cervix. *British Journal of Radiology*, *27*, 630–634.

Strickland, P. and Gregory, C., 1961. Rectal dose and rectal damage in the intracavitary treatment of uterine cancer. *Acta Radiologica* (*Stockholm*), *56*, 289–295.

Todd, T. F., 1938. Rectal ulceration following irradiation treatment of carcinoma of the cervix uteri. *Surgery Gynecology and Obstetrics*, *67*, 617–631.

Twombly, G. J., Caceres, G. H. and Corscaden, J. A., 1952. The cause, incidence and treatment of irradiation injuries in the female pelvis. *American Journal of Roentgenology*, *68*, 779–787.

Walsh, D., 1897. Deep tissue traumatism from roentgen ray exposure. *British Medical Journal*, *ii*, 272–273.

Wayte, D. M. and Helwig, E. B., 1967. Colitis cystica profunda. *American Journal of Clinical Pathology*, *48*, 159–169.

Wigby, P. E., 1943. Post-irradiation stricture of rectum and sigmoid following treatment for cervical cancer. *American Journal of Roentgenology*, *49*, 307–320.

1981, *British Journal of Radiology*, *54*, 255–257 MARCH 1981

Technical notes

A phantom for assessing the resolution at depth of a gamma camera system

By F. C. Gillespie, B.Sc., PhD., F.Inst.P.

West of Scotland Health Boards, Department of Clinical Physics and Bio-Engineering,
11 West Graham Street, Glasgow G4 9LF

(*Received September 1980*)

The normal semi-quantitative method of assessing the resolution of a gamma camera system is to use either a standard Anger pie phantom (Anger, 1973) or a lead bar phantom placed on the camera's collimator face and illuminated by an extended plane source of radioactivity. Additional information regarding resolution at depth may be obtained by the tedious procedure of interposing various thicknesses of absorber between phantom and collimator, as recommended by the Hospital Physicists' Association (HPA, 1978). This method is open to abuse since gamma camera and photographic settings can be repeatedly changed to ensure optimum results at the various depths—a procedure not applicable in normal clinical practice where in effect all depths are viewed simultaneously.

Hine *et al.* (1977) have developed a phantom for assessing spatial resolution at various depths from a single exposure. The phantom, which may be filled with water, comprises an array of parallel line sources inclined at an angle of 45° to the collimator face. This phantom overcomes some of the disadvantages of the more tedious methods of assessing spatial resolution at depth, but suffers itself from the disadvantage that the microscopic count density varies greatly throughout the field owing first to variation in absorption of radiation with depth and second to the fact that line source activity is uniform and independent of source separation.

This note describes a phantom, based on the Anger concept of hexagonal arrays of holes of differing diameters and separations, which gives simultaneous readily interpretable semi-quantitative information about resolution at all depths between 0 and 10 cm and which overcomes the defect of non-uniformity of count density. The phantom, which is intended for use with ^{99}Tc^{m}, was designed for large-field gamma cameras but can, if carefully positioned, also provide information about standard-field cameras. It is normally used with the camera face-up.

APPARATUS

The system comprises three parts, (*a*) an absorber, (*b*) a lead plate with arrays of holes drilled through it and (*c*) an extended source.

The absorber is a right-angled wedge of tissue-equivalent wax (50% paraffin wax, 50% beeswax) encased within a plywood container (Fig. 1) with base dimensions 280 × 300 mm and with wedge angle 27°. To the sloping face of the wedge is attached a 2 mm thick rectangular lead sheet, also 280 × 300 mm. Arrays of holes are arranged in six parallel bands running from the ridge of the wedge at height 0 to a height above the base of 100 mm. The holes are drilled at right angles to the base, not normal to the sloping face, and are arranged so that their projections on the base form hexagonal arrays in which within each band the separation of the holes is four times the hole diameter. The projected arrays have hole diameters of 2, 2.5, 3, 3.5, 4 and 5 mm and separations 8, 10, 12, 14, 16 and 20 mm respectively, just as in the standard Anger phantom. They are encompassed within a total area of 210 × 240 mm which can be accommodated within the field of view of a large-field but not a standard-field camera.

The extended source is not of uniform thickness. Such an arrangement would result in the count rates attributable to sources at depth being much lower

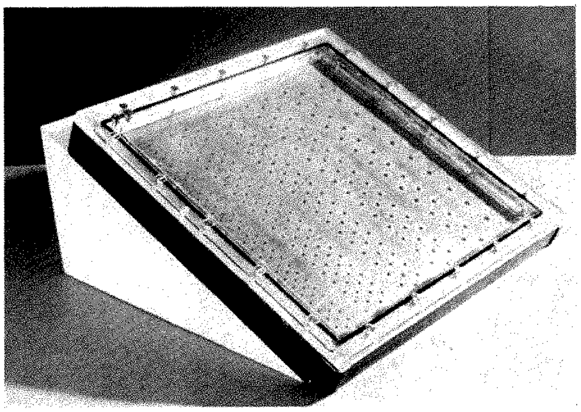


FIG. 1.

Complete system comprising wedge absorber, lead object plate with arrays of holes and extended source.

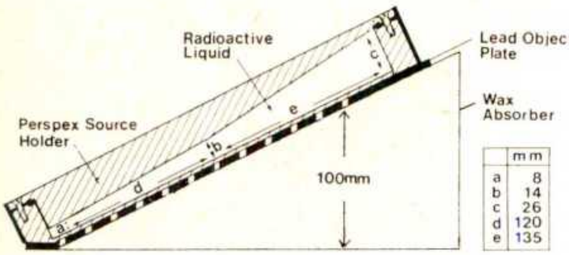


FIG. 2.

Section through system showing wedge absorber, lead object plate with holes drilled vertically to a maximum height of 100 mm and extended source of varying thickness to compensate for absorption.

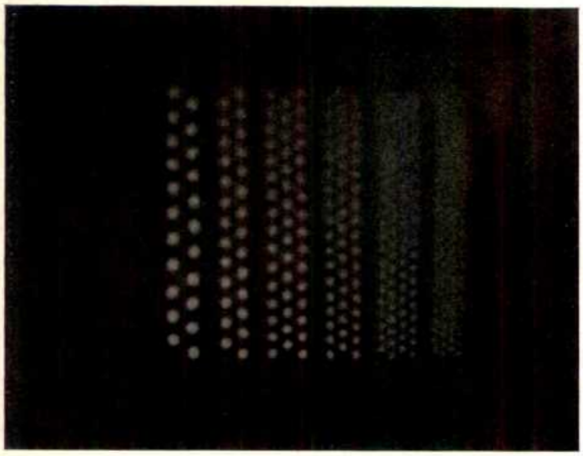


FIG. 3.

Image obtained with Ohio Nuclear large-field camera and 140 keV high-resolution collimator. 10^6 counts were obtained in 14 min using 600 MBq (16 mCi) ^{99}Tc^{m}. Holes are at zero depth at bottom and 100 mm depth at top. In the original the fifth band (2.5 mm diameter) was resolved to 70 mm depth and the sixth band (2 mm diameter) to 40 mm depth.

than to corresponding sources at the surface. Instead the source thickness is non-uniform and is designed to compensate for attenuation in the absorber. The thickness of the source should in theory increase in the appropriate exponential manner to achieve this. In practice, for ease of construction, the ideal exponential cross-section is approximated by two straight lines (Fig. 2).

The source is a radioactive liquid kept within a rectangular Perspex container with inner dimensions 255 × 255 mm and with thin 2 mm lead side walls to absorb scattered radiation. The Perspex lid of the container is sealed with a rubber "O" ring. Inlet and air outlet sealable screws are provided to allow the introduction of radioactive liquid. The Perspex source holder is kept in position on the face of the lead plate of the phantom using two locating pins attached to the plate.

RESULTS

The image obtained using an Ohio Nuclear large-field camera (type 410 with VIP 450) and 140 keV high-resolution parallel-hole collimator is shown in Fig. 3. The image, which contains 10^6 counts, was obtained in approximately 14 min using 600 MBq (16 mCi) ^{99}Tc^{m}. The apertures seen at the bottom of the image are at zero depth, those at the top at 100 mm depth. Sources in the first four bands are readily resolved at all depths. In the original photograph, those in the fifth band (2.5 mm diameter, 10 mm separation) were resolved to a depth of about 70 mm and those in the sixth band (2 mm diameter, 8 mm separation) to a depth of about 40 mm.

The variation in count rate within a 10 mm square area with the lead plate removed but with source and wedge in place was less than ±8%, due correction having been made for the inherent non-uniformity of the camera. This showed that the compensation for increasing absorber attenuation with depth achieved by using an increasing source thickness was effective.

DISCUSSION

The phantom described here gives readily interpretable semi-quantitative information about the resolution of a gamma camera system at depths between 0 and 100 mm. Use of the same set of hole diameters and separations as in the standard Anger phantom ensures rapid understanding of the method and aids assessment of the significance of the results. The compensated extended source ensures that all parts of the image contain approximately the same number of events.

Similar phantoms could be constructed for use with standard-field cameras by reducing the number of rows of holes in each band and by increasing the angle of the wedge, these procedures having the effect of reducing the image size. It should, however, be noted that the present phantom can be used with a standard-field camera provided its location on the face of the collimator is adjusted so that the important areas (those at the limit of resolution) are within the field. A similar phantom for use with higher-energy γ rays would require a thicker lead plate and thicker lead shielding. Modifications would also have to be made to the source since the compensation factors depend on γ-ray energy.

The phantom is convenient to use and its construction is not unduly complex.

ACKNOWLEDGMENTS

The author is indebted to Mr. J. S. Paton and Mr. R. Donnet for technical advice, to Mr. R. Laing for constructing the phantom and to Dr. R. Railton, Dr. D. J. Sumner, Dr. P. W. Horton and Mr. A. Eadie for using it to test their gamma cameras.

REFERENCES

ANGER, H. O., 1973. Testing the performance of scintillation cameras. *U.S. Atomic Energy Commission Report* LBL-2027, UC-37 Instruments, TID-4500.

HINE, G. J., PARAS, P. and WARR, C. P., 1977. Measurement of the performance parameters of gamma cameras, Part 1. *U.S. Department of Health, Education and Welfare, Report* FDA 78–8049.

HOSPITAL PHYSICISTS' ASSOCIATION, 1978. The theory, specification and testing of Anger type gamma cameras. *HPA Topic Group Report 27.*

Personalized fixation using a vacuum consolidation technique

By C. W. Dickens, M.I.S.T.

Department of Radiotherapy and Oncology, The Royal Marsden Hospital, Downs Road, Sutton, Surrey

(Received October 1980 and in revised form November 1980)

The exact daily repositioning of patients on radiotherapy, simulator or computed tomography couches has always caused concern. The practical difficulties of good whole-body location have in the past been compounded by the imprecise fixation methods available for this purpose, *i.e.* sand bags, couch props, etc. Stabilization of the head and neck has been achieved by use of the beam-direction shell which experience has shown, when fitted accurately to bony locations, to be eminently suitable for small, multiple-field treatments.

However, where larger volumes are involved and precise scanning or treatments are difficult due to the large amount of mobile tissue involved, especially in the abdomen, the indirect technique of the transparent beam shell becomes time-consuming and cumbersome and is very difficult to fit accurately.

Movement of the patient during treatment of extended fields has been noted and a system devised to eliminate this (Johnson and Collins, 1971). Others (Walbom-Jorgenson *et al.*, 1972) introduced individually-made expanded polystyrene boxes, using foaming isocyanates as a shaping medium. Both systems, whilst making a significant contribution towards the elimination of movement, involved toxic chemical reactions and, if not used with great care, could present a hazard to both patient and technician. Recent legislation in the United Kingdom forbids the use of isocyanates without adequate ventilation and protective clothing, making it difficult to use for work with patients. Later, lightweight plaster was used to avoid the toxicity of isocyanates (Johnson and Collins, 1971).

The system about to be described overcomes some of the problems mentioned and still provides a rigid, personalized shaped block with greater comfort for the patient than hitherto.

DESCRIPTION OF SYSTEM

The vacuum consolidation technique employs an airtight bag filled with a granular material which, when held against a contour whilst being evacuated, takes the shape of that contour in negative form. The granules lock together under the influence of atmospheric pressure to form a rigid shape and maintain that shape whilst pressure is being applied.

This principle is made more versatile and permanent by the use of an extremely thin flexible bag partially filled with expanded polystyrene beads, plus a heat-sensitive co-polymer (Revinex 83 MIO, Revertex Ltd., Harlow, Essex). The evacuated bag can then be made a permanent shaped block by closing a valve fitted to the bag, disconnecting from the supply, and heat curing for one hour at 50°C—an irreversible process.

After cure the vacuum can be released and the resultant form is rigid, light to carry, with a specific gravity of 0.044, translucent to X-rays, yet durable enough to last a full course of radiotherapy treatment or a prolonged diagnostic procedure.

Method of use

The patient is placed in position on the couch, supported either on a bag or alongside one. Gentle pressure is applied to the outside of the bag by the operator's hands, and the vacuum gently but simultaneously applied. When the bag has been pushed into full contact with the patient, the vacuum is increased to 250 Torr and held for one minute. Subsequent alterations in position can be made by

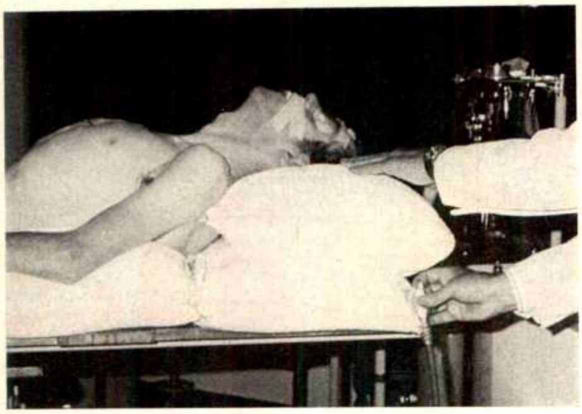


FIG. 1.
Patient in position and bags being evacuated.

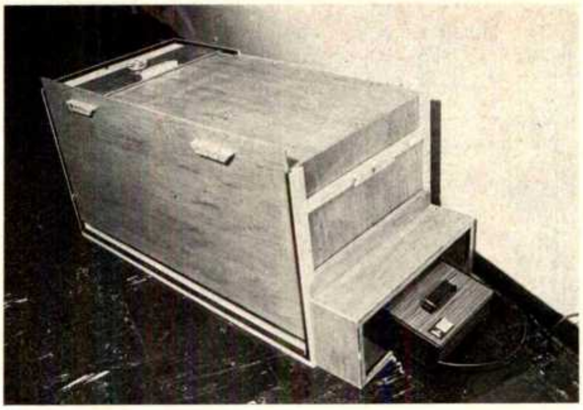


FIG. 2.
Hot air cabinet.

releasing the vacuum and re-positioning the patient, and the procedure may be repeated any number of times until correct.

Depending on need, bags can either be evacuated against the patient and surface of the couch, or fixed to it by laying the bag first over locating battens on the surface or side of the couch around which the bag will form during the pressure reduction. No significant dimensional change has been noticed when patient, bag and couch support are re-united after cure.

Experience over the past eight months has shown the technique to be successful when used to improve localization of the large-field mantle treatments, and for supporting breast patients being treated by tangential fields. Work is in hand to determine the ideal shape of bag and amount of filling required for infants normally sedated whilst the whole CNS is irradiated. Ultimately, a uniform system of whole-body immobilization will evolve to ensure reproducibility of the patient on CT scanner, simulator and radiotherapy treatment machine.

Vacuum

Where installed, hospital vacuum systems have proved adequate to deal with any number of small bags. The co-polymer used, a non-toxic substance, is stated by the manufacturers to comply with the Food and Drugs Administration (USA) Regulations and, provided a trap separator is installed, no harm will come to the vacuum system.

Alternatively, we have found a trolley-mounted rotary vacuum pump fitted with a foot control valve is more versatile. It can be moved into position near the couch in the treatment or simulator rooms, leaving both hands free to compact the bag around the patient (Fig. 1).

Oven

A simple, hot-air cabinet, size 120×60×60 cm (Fig. 2), has adjustable slides for regulating the airflow which have been found to be very efficient in operation. It uses a standard domestic turbo fan heater thermostatically controlled which maintains an airflow over the bags at the required temperature.

ACKNOWLEDGMENTS

The author wishes to record with appreciation the technical assistance and co-operation given by Mr. M. C. Bailey (Revertex Ltd.), whose help in selecting a suitable co-polymer proved invaluable.

REFERENCES

JOHNSON, R. J. R. and COLLINS, C., 1971. Immobilisation of patients during wide-field radiotherapy. *British Journal of Radiology*, *44*, 724–727.

WALBOM-JORGENSON, S., CLEEMAN, L., NYBO-RASMUSSEN, A. and BYRGE SORENSEN, P., 1972. Technical aids for the radiotherapy of Hodgkin's disease. *British Journal of Radiology*, *45*, 949–953.

1981, *British Journal of Radiology*, *54*, 259 MARCH 1981

Case reports

Iodine 131 ablation therapy for a patient on maintenance haemodialysis

By N. Howard, M.A., D.M., F.R.C.R. and M. Glasser, M.B., B.S., F.R.C.R., F.F.R. (R.C.S.I.)

Department of Radiotherapy and Oncology, Charing Cross Hospital, London

(*Received September 1980*)

Carcinoma of the thyroid accounts for 1% of malignant disease. There are 250 new cases of papillary carcinoma of the thyroid a year, 75% of which are in female patients. There are approximately 650 new female patients starting on maintenance haemodialysis each year. From this it is evident that the need for ^{131}I ablation therapy for a patient on maintenance haemodialysis is extremely rare.

The following description illustrates the problems involved in administering radionuclides to patients with abnormal excretion and distribution of these substances. We discuss the methods evolved to solve this extremely unusual problem—unique in our experience.

CASE REPORT

A 34-year-old female patient was referred to the radiotherapy department of this hospital in October 1974. She had been on maintenance haemodialysis since January 1974 because of chronic renal failure, thought to be caused by recurrent upper urinary tract infections in childhood.

The patient had a symptomless thyroid nodule which she noticed in 1972. It had recently become enlarged. There was no pain, voice changes, or symptoms of thyrotoxicosis. A sub-total thyroidectomy was performed a week before referral on 22 November 1974. The calcified nodule seen previously on thyroid scans was found histologically to be a papillary carcinoma of the thyroid.

It is our policy to give an ablation dose of radioiodine following surgery, even if removal is thought to be total, as there is usually a small remnant of normal thyroid remaining, as can be shown on thyroid scanning. We give a 3.0 GBq (80 mCi) ablation dose of radioiodine and scan two months later. If clear that is the end of active treatment. If there is uptake, it cannot be known if this is normal thyroid or tumour, and a therapy dose of 5.6 GBq (150 mCi) radioiodine is given. This is repeated two monthly until there is no further uptake.

We therefore decided to give this patient a radioiodine dose equivalent to 3.0 GBq (80 mCi) and the following investigations were performed. It should be added that a review of the literature recorded no comparable case and we therefore had to work from first principles.

Thyroid uptake

(1) at 24 hours, 6% of dose; (2) at 48 hours, 10% of dose. Conclusion: definite therapeutic benefit to be expected from the uptake between 24 and 48 hours.

Body loss of radioiodine

Urinary excretion, 5% in 24 hours. Clearance by dialysis (estimated from sampling of dialysate, plasma radioiodine whole-body counting) 90% in 10 hours.

Calculation of radiation dose from radiotherapy records

The persistence of radioiodine in four otherwise normal subjects was estimated from external dose-meter records. The dwell time of radioiodine in the body (in millicurie hours) in the patient was likely to be 2½ times that of a "normal" subject if dialysed after 24 hours, and 4½ times if dialysed after 48 hours.

DISCUSSION

The best therapeutic approach seemed to be to arrange dialysis 48 hours after the dose, and to reduce the dose given by a factor of 4. The initial dose, therefore, was 740 MBq (20 mCi) ^{131}I. This gave whole-body irradiation comparable to a dose of 3.0 GBq (80 mCi) in otherwise normal subjects, and probably greater irradiation of the thyroid.

The patient continued on maintenance haemodialysis, remaining reasonably well. In October 1976 she underwent a left renal transplant, which was rejected. Repeated whole-body ^{131}I scans consistently showed no uptake or evidence of tumour. In July 1979 she developed impairment of vision and a diagnosis of retrobulbar neuritis was made. Isotope brain scan and computerised tomography of the brain were normal. She developed further neurological abnormalities and continued to deteriorate and died on 19 August 1979. Post-mortem examination revealed no evidence of tumour anywhere in the body. The cause of death was thought to be an opportunist or viral infection although the organism could not be identified.

ACKNOWLEDGMENTS

Our thanks are due to Mr. A. R. Makey, Dr. R. Jewkes and Miss B. E. Jones, and to Miss C. Paxton for typing the paper.

1981, *British Journal of Radiology*, *54*, 260–261

Case reports

Intermittent cyanotic attacks in an infant—an unusual presentation of a congenital anterior diaphragmatic (Morgani) hernia

By M. D. Cohen, M.R.C.P., F.R.C.R., M.D.

Department of Radiology, Leeds General Infirmary, Leeds LS1 3EX

(*Received August 1980*)

Morgani (anterior diaphragmatic) hernias are uncommon. They rarely cause symptoms and are usually discovered as an incidental finding (Kendig, 1977). This report discusses an infant in whom episodic herniation of bowel through an anterior diaphragmatic defect caused intermittent cyanotic attacks.

CASE REPORT

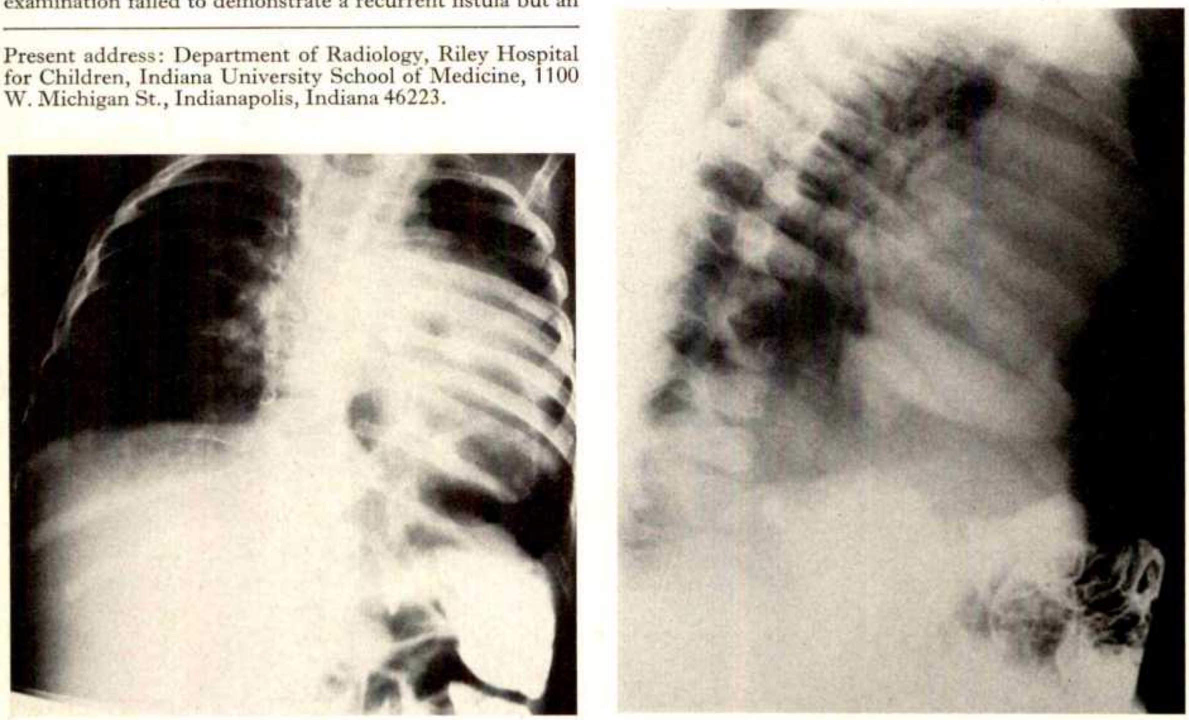
A six-month-old boy presented with intermittent cyanotic attacks. Previously an oesophageal atresia, diagnosed shortly after birth, had been repaired and a distal tracheo-oesophageal fistula had been closed surgically. Also noted were: a single umbilical artery, a single right kidney, multiple rib deformities, and abnormalities of the thoracic vertebrae. Dilatation of the oesophagus had been performed several times in the first two months of life following stenosis at the site of anastomosis and the boy had suffered several episodes of aspiration pneumonia.

The cyanotic attacks, which had occurred from the first weeks of life without evidence of cardiac abnormality, persisted and occasionally were related to feeding. Barium examination failed to demonstrate a recurrent fistula but an abnormal lucency was noted low in the anterior mediastinum on fluoroscopy and this was confirmed on frontal and lateral chest radiographs, Fig. 1, A and B. A repeat film, Fig. 2, taken ten minutes later showed spontaneous resolution of the abnormal gas shadows. In retrospect a film, Fig. 3, taken at the age of one month showed a similar mediastinal gas shadow.

At operation a 5.0 cm diameter defect was found in the diaphragm mainly to the left side with a hernia sac present. This Morgani hernia was repaired with relief of the cyanotic attacks.

DISCUSSION

Morgani hernias are hernias through a congenital defect in the anterior part of the diaphragm (Kendig, 1977). These defects are gaps on each side of the sternal muscle strip of the diaphragm. Whilst the defect is usually on the right, it can be on the left or there can be a single large midline anterior defect (Jemerin, 1963).



A

FIG. 1.

B

Age six months. There is a collection of gas shadows seen overlying the heart on the frontal view and just behind the lower sternum on the lateral view.

Present address: Department of Radiology, Riley Hospital for Children, Indiana University School of Medicine, 1100 W. Michigan St., Indianapolis, Indiana 46223.

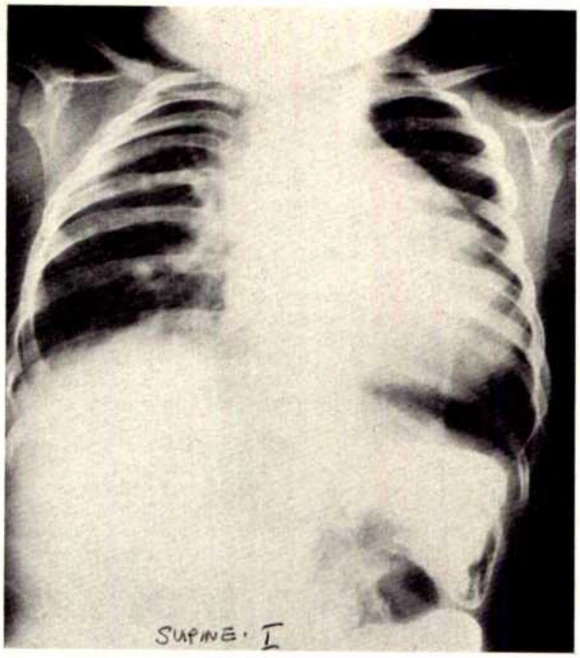


FIG. 2.
Age six months. Taken ten minutes after Fig. 1. The gas shadows are no longer seen overlying the heart.

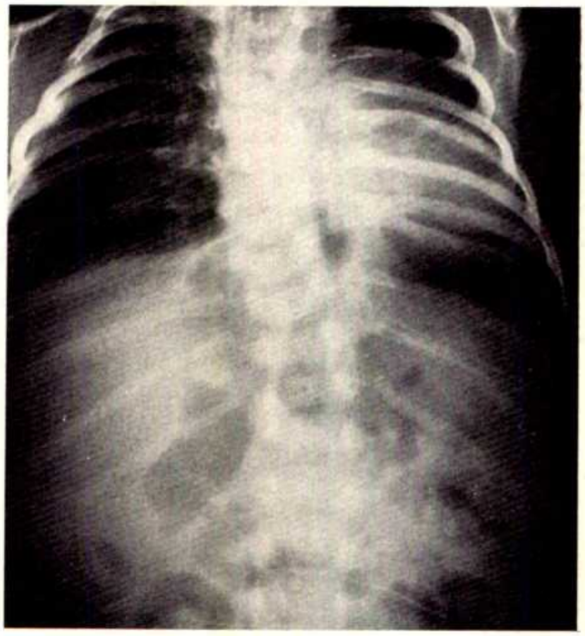


FIG. 3.
Age one month. Routine chest radiograph taken following repair of an oesophageal fistula. The central gas shadow in the upper abdomen/lower chest is herniated bowel.

Morgani hernias are rare. The incidence has been estimated at between 1% (Kendig, 1977) and 5% (Bentley and Lister, 1965) of all congenital diaphragmatic hernias. Posterior (Bochdalek) diaphragmatic hernias are the commonest congenital diaphragmatic hernia. They usually produce early severe respiratory symptoms and are thus diagnosed in the neonatal period (Rickham *et al.*, 1978). Morgani hernias on the other hand usually do *not* produce any symptoms (Kendig, 1977; Caffey, 1973; Swischuk, 1978). They are *not* diagnosed at an early age, but commonly are found as an incidental finding on a chest radiograph in an adult (Jemerin, 1963; Hajdu and Sidhva, 1955). In the rare cases in which Morgani hernias have caused symptoms, these have been reported as vomiting, abdominal pain, dyspnoea or cough (Kendig, 1977; Boyd, 1961; Baran *et al.*, 1967) but not as intermittent cyanosis. One series of eight cases seen over a period of 20 years is reported from Liverpool (Thomas and Clithero, 1977). Four of the cases presented with respiratory distress shortly after birth. The other four cases presented from three weeks to eight years of age with recurrent chest infections or vomiting. Morgani hernias are usually on the right side (Baran *et al.*, 1967). The case presented above had a left-sided hernia. It may be that the cyanotic attacks were due to interference with cardiac function by the left-sided hernia compressing the heart.

REFERENCES

BARAN, E. M., HOUSTON, H. E., LYNN, H. and O'CONNELL, E. J., 1967. Foramen of Morgani hernias in children. *Surgery*, *62*, 1076–1081.

BENTLEY, G. and LISTER, J., 1965. Retrosternal hernia. *Surgery*, *57*, 567–575.

BOYD, D., 1961. Diaphragmatic hernia through the foramen of Morgani. *Surgical Clinics of North America*, *41*, 839–846.

CAFFEY, J., 1973. *Pediatric X-ray Diagnosis.* 6th ed. (Yearbook Medical Publishers, Chicago), pp. 560–561.

HAJDU, N. H. and SIDHVA, J. N., 1955. Parasternal diaphragmatic hernia through the foramen of Morgani. *British Journal of Radiology*, *28*, 355–357.

JEMERIN, E., 1963. Diaphragmatic hernia through the foramen of Morgani. *Journal of the Mount Sinai Hospital*, *30*, 415–426.

KENDIG, E. L., 1977. *Disorders of the respiratory tract in children.* 3rd ed. (Saunders, Philadelphia), p.218.

RICKHAM, P. P., LISTER, J. and IRVING, I. M., 1978. *Neonatal Surgery.* 2nd ed. (Butterworth, London), p. 164.

SWISCHUK, L. E., 1978. Acute respiratory distress in the infant. *Radiological Clinics of North America*, *16*, 77–90.

THOMAS, G. C., and CLITHERO, N. 1977. Herniation through the foramen of Morgani in children. *British Journal of Surgery*, *64*, 215–217.

1981, *British Journal of Radiology*, *54*, 262

A calcified renal mass: chondrosarcoma of kidney

Jean Pitfield, M.B., Ch.B., D.M.R.D., F.R.C.R., B. J. Preston, M.B., D.M.R.D., F.R.C.S. (Ed), F.R.C.R. and P. G. Smith, M.B., B.S., F.R.C.Path.

Departments of Diagnostic Radiology and Histopathology, University Hospital, Nottingham

The location of calcification within a renal mass has often been related to its pathology (Daniel *et al.*, 1972). A large renal mass with both rim and amorphous calcification was unexpectedly found to be chondrosarcomatous. This appears to be a very rare tumour, previously reported in association with transitional cell carcinoma of kidney (Gallagher *et al.*, 1974).

CASE REPORT

In April, 1973, a 61-year-old white male presented with severe left loin pain of two months' duration. The pain was constant, radiated to his umbilicus and was associated with dysuria and frequency. On examination, he was found to have a large tender mass in the left flank. He weighed 86.9 kg and had a haemoglobin of 11.2 g with a normochromic normocytic picture. His ESR was 113 mm per hour.

A plain abdominal radiograph (Fig. 1) and an excretion urogram showed massive enlargement of a non-functioning left kidney. There was a calcified rim around the lower pole of the renal mass and scattered amorphous calcification within its substance. A provisional diagnosis of renal cell carcinoma was made and angiography was performed. This showed the aorta to be displaced to the right with stretching of the left main renal artery and its branches. No pathological circulation was demonstrated.

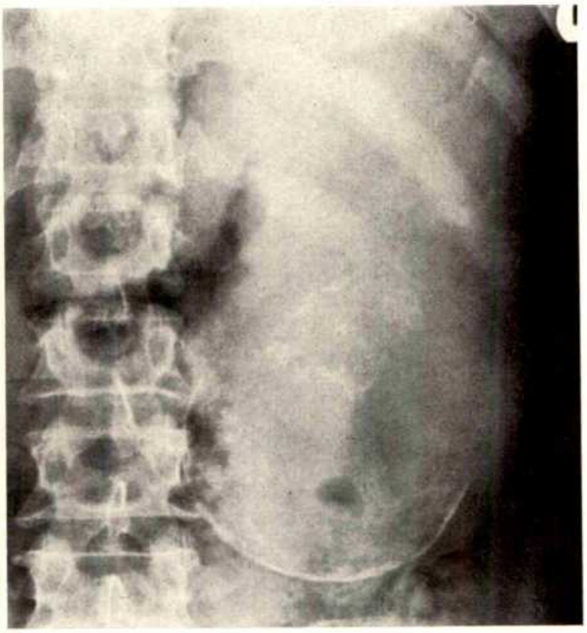


FIG. 1.

Plain abdominal radiograph showing a large calcified left renal mass.

Left uretero-nephrectomy was performed with difficulty, leaving a plaque of tumour attached to the left psoas muscle.

The resected specimen was a large bossellated mass measuring 23 × 18 × 14 cm and weighing 2145 g. Part of the surface was recognizable as kidney which was considerably expanded (18 × 12 × 11 cm). The cut surface of the mass and much of the kidney was very firm with necrotic, haemorrhagic, cystic and calcified foci. Histology showed numerous small islands of well differentiated cartilage surrounded by spindle cells in an extensively necrotic tumour. Cartilaginous elements are occasionally seen in renal tumours, especially transitional cell carcinoma (Gallagher *et al.*, 1974) but extensive review of this case showed no evidence of any other tissue. The appearances indicated a primary chondrosarcoma of the kidney.

At follow-up, one month post-operatively, the patient complained of further severe left loin pain and was found to have recurrent tumour in his operation wound, together with a large underlying mass. He died three weeks later.

DISCUSSION

Of the 2709 renal masses reviewed by Daniel *et al.* (1972) at the Mayo Clinic, 23 showed a combination of both peripheral and non-peripheral calcification. Approximately 70% of the lesions in this combination group proved to be benign. This patient had a large calcified renal mass due to chondrosarcoma of kidney. This cause of renal calcification is an addition to the long list of aetiologies previously mentioned in the literature.

ACKNOWLEDGMENTS

We would like to thank Mr. H. H. Renyard, the Consultant Surgeon in charge of the case, and the Department of Medical Photography of the University Hospital, Nottingham. We also thank Mrs. Stagg of the City Hospital, Nottingham and Mrs. Shury of Guy's Hospital, London for typing the manuscript. We are grateful to Dr. H. M. Saxton for his helpful comments.

REFERENCES

DANIEL, W. W., HARTMAN, G. W., WITTEN, D. M., FARROW, G. M. and PANAYOTIS, P. K., 1972. Calcified renal masses: a review of ten years experience at the Mayo clinic. *Radiology*, *103*, 503–508.

GALLAGHER, J. C., WINSLOW, D. J. and GROSSMAN, A., 1974. Coexistent chondrosarcoma and transitional cell carcinoma in kidney. *Urology*, *3*, 473–477.

1981, *British Journal of Radiology*, 54, 263–265 MARCH 1981

Case reports

Computed tomography in diabetes insipidus: posterior empty sella

By *G. D. Marano, M.D., *J. A. Horton, M.D. and †A. M. Vazquez, M.D.

Department of *Radiology and †Pediatrics, West Virginia University School of Medicine

Neurogenic diabetes insipidus (DI) is due to a deficiency of circulating antidiuretic hormone (ADH) with subsequent excessive renal water loss. The differential diagnosis includes idiopathic (familial or congenital), post-traumatic, granulomatous disease (sarcoidosis, tuberculosis, syphilis), histiocytosis X, neurosurgical intervention, vascular lesions (*e.g.* aneurysm of anterior communicating artery, post-partum pituitary necrosis), pyogenic infection, and tumours (*e.g.* glioma, craniopharyngioma) (Baker and Baker, 1978; Martin *et al.*, 1977). However, empty sella syndrome has only rarely been reported with DI (Cuppo and Woolf, 1979; Manelfe and Louvet, 1979; Matisonn and Pimstone, 1973; Schaison and Metzger, 1976). Manelfe *et al.* (1978; 1979) recently described their computed tomographic (CT) findings in 13 patients with diabetes insipidus. One of their patients had an empty sella plus amenorrhoea and galactorrhoea. Recently we have had the opportunity to investigate by routine CT and CT metrizamide cisternography two patients with neurogenic DI, in whom the finding of a posterior empty sella was demonstrated.

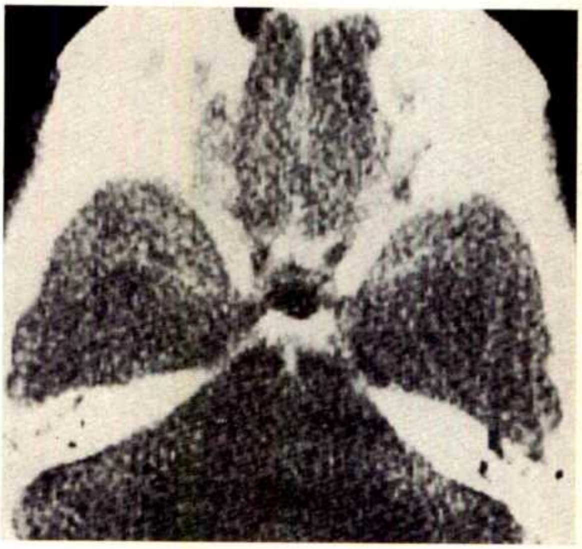


FIG. 1.

Enhanced scan of Case 1 through the sella turcica with low density seen in the posterior aspect and tissue density in the anterior portion.

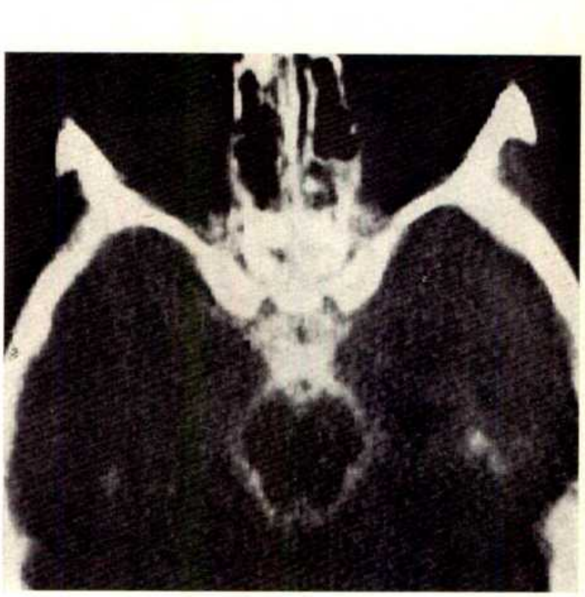


FIG. 2.

Metrizamide cisternogram of Case 1 shows opacification of the subarachnoid space and particularly in the intrasellar cistern.

CASE 1

A five-year-old adopted white male presented with a history of polydipsia and polyuria since age five months. The past history was negative for head trauma, severe febrile illness, seizures or neurological abnormalities. Family history was not available. Growth and development were normal. Physical examination revealed the height of 115 cm. (50th percentile) and the weight 23.2 kg (90th percentile). Eyegrounds were normal. Visual field examination was attempted, but it was unsuccessful. The remainder of the physical examination was normal. The haemogram was normal. Urinalysis revealed a specific gravity ranging from 1.001 to 1.003. Blood electrolytes and glucose were normal. The bone age according to the standards of Greulich and Pyle (1959) was five years. Skull films and coned-down views of the sella turcica were normal. CT scan with and without contrast enhancement demonstrated absence of pituitary tissue in the posterior aspect of the sella (Fig. 1). A CT metrizamide cisternogram demonstrated filling of the previously empty region of the sella with contrast material (Fig. 2). After water deprivation for six hours there was failure to concentrate the urine and the urine osmolality was 84 mOsm/kg. After 0.05 ml of DDAVP the urine specific gravity rose to 1.015 and the osmolality to 498 mOsm/kg. Plasma ACTH levels before and after metyrapone adminstered p.o. were 25 and 218 pg/ml respectively. Serum prolactin was 4.7 ng/ml, serum T4 12.8 μg/dl and serum TSH 3.3 μU/ml. The peak growth hormone concentration after combined L-Dopa arginine stimulation was 9.8 ng/ml. The patient was dis-

---

Address for reprints: Gary D. Marano, M.D., West Virginia University, Department of Radiology, Morgantown, WV 26506.

charged on treatment with DDAVP 0.05 ml intranasally once daily. In essence, this child's anterior pituitary function was intact; but he had diabetes insipidus secondary to absence of the neurohypophysis.

CASE 2

A 14½-year-old male was hospitalized at West Virginia University Hospital on October 4, 1976 with a four-month history of polyuria and polydipsia. He was the product of a 38-week gestation and the labour was precipitous. He developed hyaline membrane disease which required intensive therapy for 72 h. His birth weight was 2580 g. At two years he underwent surgery for ptosis of the left eye. At six years he was hospitalized for acute asthmatic bronchitis. His early childhood was characterized by many allergies. Despite this his growth and development were normal and he has always performed extremely well in school. At ten years he developed early pubertal changes and was considered to be at stage II on the Tanner scale. Two male siblings had the onset of puberty at ages 16 and 14 years. When he was hospitalized for polyuria and polydipsia, no history of head trauma or headache was elicited. Height and weight were at the 25th and 75th percentiles respectively. Physical examination and neurological assessment were normal. Visual fields were intact. Bone age using the standards of Greulich and Pyle (1959) was 13 years. Skull films and coned-down views of the sella were normal. CT scan of the head revealed lack of tissue in the posterior sella. The diagnosis of idiopathic neurogenic DI was established on the basis of the responses to water deprivation and pitressin administration. He was discharged on intranasal lysine vasopressin to be followed at the paediatric endocrine clinic. At 12 years 3 months his height was plotted at the 5th percentile and weight at the 50th percentile. Testicular volume was noted to be 6 ml (Prader standards) bilaterally, penile size was 10.6 cm but there was no further increase in the amount of pubic hair. Bone age was 13½ years. At 14 years 3 months height had dropped below the 3rd percentile and the weight was at the 25th percentile. Testicular volume had actually decreased to 3 ml bilaterally, penile size 7.8 cm and only scanty pubic hair was present. His bone age was 14 years.

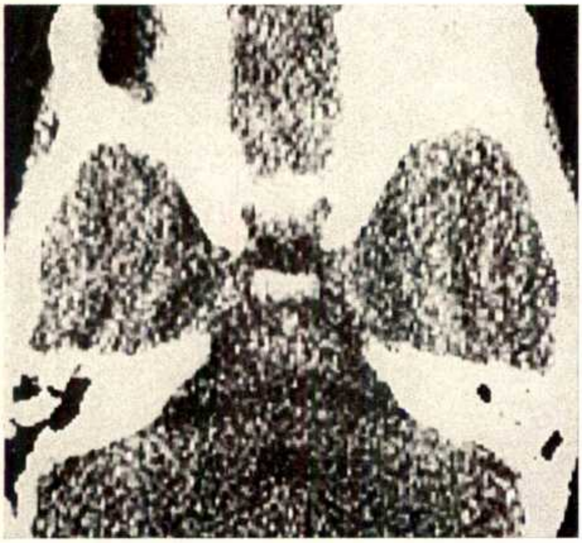


FIG. 3.

Enhanced scan of Case 2 at age 14 years through sella turcica in which anterior clinoids and dorsum are clearly demonstrated. Note as in Fig. 1 low density in the posterior aspect of the sella.

In view of the fact that growth had practically ceased and secondary sexual development had regressed he was hospitalized for test of anterior pituitary function. The physical examination was normal except for the previously described abnormalities. Neurological assessment was normal.

Endocrine studies were performed. Results are as follows: serum TSH, 3.4 mU/ml; serum T4, 8.6 μg/dl; serum testosterone concentrations before and after human chorionic gonadotropin 2000 uIM daily for three days were 58 ng/dl and 122 ng/dl respectively; plasma prolactin, 11.5 ng/ml; plasma cortisol (8 a.m.), 15.6 μg/dl; base-line urinary 13 KS and 170 HCS were 8.7 and 7.0 mg/day respectively. After p.o. metyrapone, these rose to 27.7 and 33 mg/day respectively; plasma ACTH (8 a.m.), 21 pg/ml; plasma FSH and LH were 2.3 and 3.3 mU/ml respectively.

Base-line growth hormone concentration was 1.4 ng/ml and after L-DOPA arginine stimulation the peak concentration was 1.6 ng/ml. Base-line and stimulated GH concentrations during an exercise test were 1.1 and 1.5 ng/ml respectively.

Skull films and coned-down views of the sella were still normal. Skeletal survey was normal. A CT evaluation of the head with and without enhancement demonstrated absence of pituitary tissue in the posterior aspect of the sella (Fig. 3). Subsequent CT metrizamide cisternogram demonstrated filling of the previously empty region of the sella with contrast (Fig. 4).

In summary, this 14½-year-old male has a posterior empty sella with concomittant neurogenic DI. But in addition, he has disturbed anterior pituitary function with selective involvement of growth hormone and gonadotropin secretions.

DISCUSSION

The occurrence of empty sella syndrome and DI is rare with only five reported cases in the literature (Cuppo and Woolf, 1979; Manelfe and Louvet, 1979; Matisonn and Pimstone, 1973; Schaison and

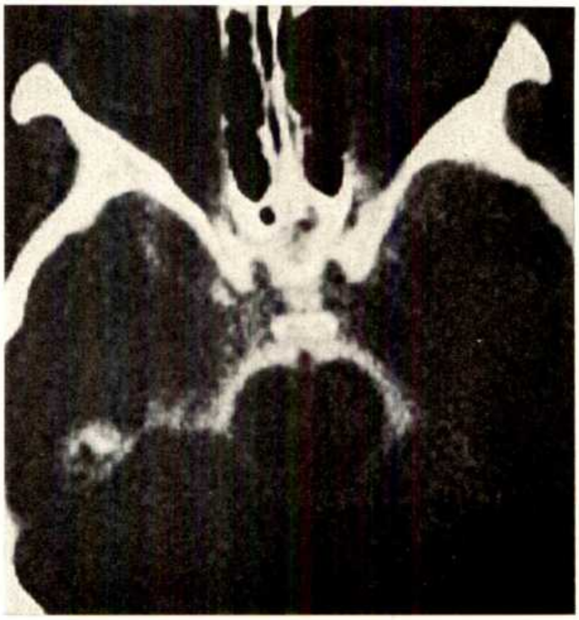


FIG. 4.

Metrizamide cisternogram of Case 2. Contrast material is in the intrasellar cistern.

Metzger, 1976). In none of these cases was DI the only endocrine dysfunction of the pituitary identified. In particular, Manelfe and Louvet (1979) reported a case of a 30-year-old woman with associated amenorrhoea galactorrhoea syndrome in which pneumoencephalography demonstrated an intrasellar cistern with pituitary tissue in the usual infero-posterior aspect of the sella turcica. Schaison and Metzger (1976) reported two female patients (ages 23 and 35 years) who also had DI with amenorrhoea galactorrhoea and similar intrasellar cisternal herniation. Matisonn and Pimstone (1973) reported a case of a 43-year-old female with DI who also had panhypopituitarism; CT scan was reported as normal but pneumoencephalography demonstrated that the sella was 90% occupied by gas, primarily in the anterior aspect.

In the two cases we present, the portion of the sella turcica that is noted to be empty is posterior with anterior pituitary tissue well demonstrated on CT. CT metrizamide cisternography shows filling of the sella with contrast; thus confirming intrasellar extension of the subarachnoid space. This varies from the above reported cases in that usually residual pituitary tissue is located inferiorly and/or posteriorly (Bush, 1951; Neelon *et al.*, 1973).

We demonstrated intact anterior pituitary function in one patient and dysfunction in the second patient.

Manelfe and Louvet (1979) in their review of 13 patients studied by CT scan did not demonstrate the posterior empty sella. In their series pneumoencephalogram was performed in six patients and CT metrizamide cisternography in one patient with only one case of empty sella being demonstrated. The primary CT abnormalities included a small round mass in the chiasmatic cistern which enhanced. This was not found in the presently reported cases. Aubin *et al.* (1978) demonstrated enlargement of the pituitary stalk with CT metrizamide cisternography in three of 12 cases of DI.

It is tempting to postulate that the CT findings in the five-year-old patient are specific for the isolated primary idiopathic (familial) form of DI (Blotner, 1958). Unfortunately, the familial nature of the disorder in this patient is unsupported due to lack of family history. In idiopathic DI, the neurohypophysis as well as supraoptic and paraventricular nuclei are atrophic (Blotner, 1958; Green *et al.*, 1967). In particular, in three autopsied cases Blotner reported significant reduction in size of the posterior lobe of the pituitary gland in two cases and a smaller than normal pituitary in the other case. Thus the posterior pituitary may be reduced in size with DI, and it is reasonable to expect the creation of a potential space into which the subarachnoid space can herniate with a resulting posterior intrasellar cistern.

REFERENCES

Aubin, M. L., Bentson, J. and Vignaud, J., 1978. CT of the pituitary stalk. *Journal of Neuroradiology*, *5*, 153–160.

Baker, A. B. and Baker, L. H., 1978. Disorders of the hypothalomus and pituitary gland. In *Clinical Neurology* (Harper and Row), Vol. 2, 24.

Blotner, H., 1958. Primary or idiopathic diabetes insipidus: a system disease. *Metabolism*, *7*, 191–200.

Bush, W., 1951. Die Morphalogie der Sella Turcica and ihre Beziehungen zur Hypophyse. *Virchows Archive Pathologische Anatomie*, *320*, 437–458.

Cuppo, T. R. and Woolf, P. O., 1979. Primary empty sella syndrome with panhypopituitarism, diabetes insipidus, and visual field defects. *Acta Endocrinologica*, *89*, 445–460.

Green, J. R., Buchan, G. C., Alvord, E. C. and Swanson A. G., 1967. Hereditary and idiopathic types of diabetes insipidus. *Brain*, *90*, 797–814.

Greulich, W. W. and Pyle, S. K., 1959. *Radiographic Atlas of Skeletal Development of the Hand and Wrist*, 2nd ed. (Stanford University Press).

Manelfe, C. and Louvet, J. P., 1979. Computed tomography in diabetes insipidus. *Journal of Computed Assisted Tomography*, *3*, 306–309.

Manelfe, C., Louvet, J. P., Boulard, C., Regnier, C., Rochicciolo, P. and Bayard, F., 1978. Hypothalmic pituitary changes in diabetes insipidus demonstrated by computed tomography. *Lancet ii*, 1379–1380.

Martin, J. B., Reichlin, S. and Brown, G. M., 1977. Neural regulation of water and salt metabolism. In *Clinical Neuroendocrinology* (F. A. Davis Company), 80–84.

Matisonn, R. and Pimstone, B., 1973. Diabetes insipidus associated with an empty sella turcica. *Postgraduate Medical Journal (South Africa)*, *48*, 274–276.

Neelon, F. A., Goree, J. A., Kushner, M. H. and Lebovitz, H. E., 1973. The primary empty sella: clinical and radiographic characteristics and endocrine function. *Medicine*, *52*, (2), 73–92.

Schaison, G. and Metzger, J., 1976. The primary empty sella on endocrine study in 12 cases. *Acta Endocrinologica*, *83*, 483–491.

1981, *British Journal of Radiology*, 54, 266–267

Case reports

Pneumatosis intestinalis in the small bowel of an adult—a radiological sign of a serious post-operative complication

By E. E. J. Smith, F.R.C.S., J. H. Saunders, F.R.C.S., and N. Bowley, F.R.C.R.

Departments of Surgery and Radiology, Hammersmith Hospital, London W12

(*Received June 1980*)

Pneumatosis intestinalis in the adult is usually described involving the colon and typically, it runs a benign course. This case report is of intramural gas in the small intestine of an adult, the development of which was of serious significance, and which was analogous to neonatal necrotizing enterocolitis.

CASE REPORT

A 38-year-old lady originally presented in out-patients with a three-month history of five to six watery stools per day, associated with colicky abdominal pain. Examination at that time revealed no abnormal signs. One week later, before a barium enema had been performed, she was admitted as an emergency, passing large amounts of fresh blood per rectum. Initially her cardiovascular system was stable, but she continued to bleed briskly and as a result, became hypotensive. This was corrected by blood transfusion and laparotomy was performed to arrest the haemorrhage. At operation, the small bowel was entirely normal, but the large bowel, especially on the right, was covered with abnormally dilated, grape-like vessels and the whole colon was distended with blood. A right hemicolectomy was performed, but post-operatively the patient continued to bleed and consequently returned to theatre a few hours later, when the remainder of the colon was removed. The rectal stump was closed and an ileostomy fashioned. Subsequent histology revealed venous malformations extending from serosa to mucosa along the whole length of the large bowel.

The patient initially made a satisfactory recovery, but one week post-operatively suddenly became confused. Associated with this, she also became febrile and hypotensive and her abdomen was distended, tender and without bowel sounds. Sloughs of tissue were noted in the ileostomy fluid. The white cell count was 34 300 and her urea had risen to 42.1 mmol/l (from 5.4 mmol/l three days previously). Several blood cultures failed to grow any organisms but culture of the ileostomy fluid grew *E. coli*, *Klebsiella* and *Strep. faecalis*. A plain abdominal radiograph at this time showed gross dilatation of the stomach and marked dilatation of the whole small bowel, with multiple fluid levels (Fig. 1). Of particular interest, however, were streaks of gas in the bowel wall (Figs. 1 and 2), and gas tracking along the mesentery of the small bowel.

The patient was treated conservatively with intravenous fluids and antibiotics. Her subsequent course was prolonged and stormy, with an ileus associated with a massive naso-gastric aspirate that persisted for over two weeks. She also developed a pelvic abscess that was drained through an abdominal incision, acalculous cholecystitis requiring

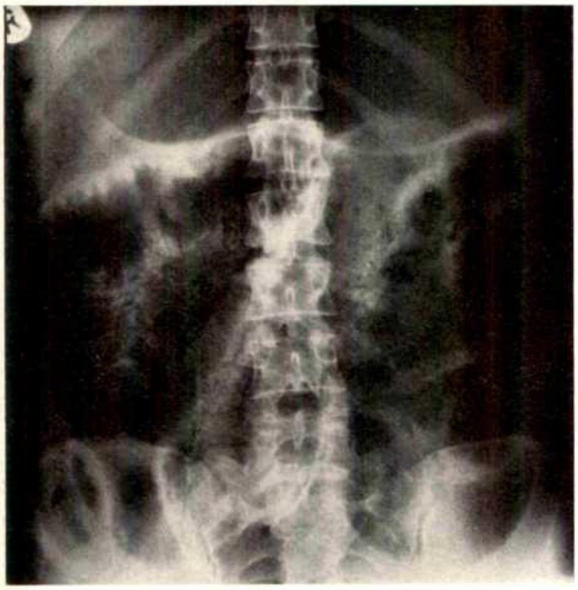


FIG. 1.

Gaseous distension of stomach and small bowel loops.

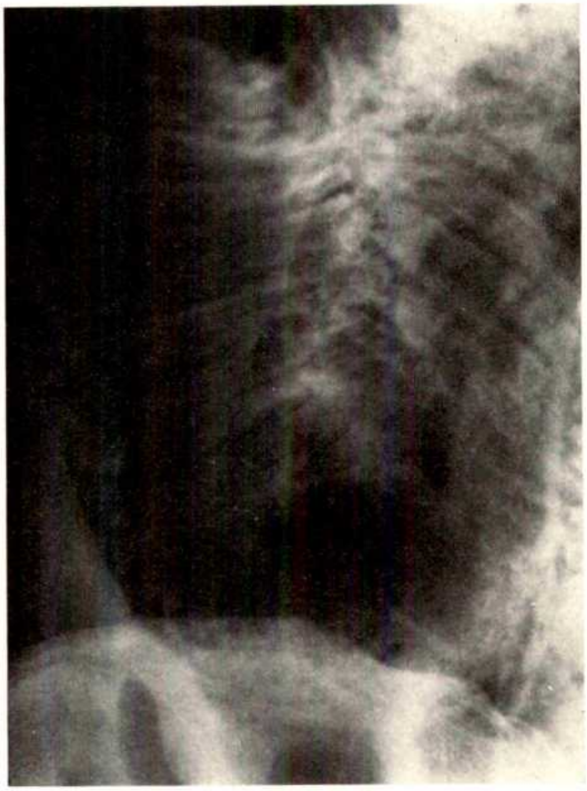


FIG. 2.

Close up of right flank revealing linear streaks of gas in a loop of small bowel.

cholecystectomy and a retroperitoneal abscess drained via the rectal stump. Eventually, however, she recovered sufficiently to be allowed home, two months after her initial operation.

COMMENT

Pneumatosis intestinalis is a rare condition, but nevertheless well described in the literature. In adults it is probably best known involving the large bowel, and although any part may be affected, rectal pneumatosis is unusual. The bubbles of gas are well defined, vary in size up to 2 cm diameter or more, occur separately or in clusters, may be subserosal or submucosal, and are characteristically cystic—hence the term pneumatosis cystoides intestinalis. The majority of cases are idiopathic, but there is a frequent association with chronic pulmonary disease when the cysts may be secondary to dissection of gas from the lungs (Hughes *et al.*, 1966).

Pneumatosis cystoides intestinalis is essentially a benign condition, often being no more than an incidental finding (Marshak *et al.*, 1956). It may, however, be responsible for colonic dysfunction (Dendy Moore, 1968) and can also cause diagnostic confusion by simulating colonic polyposis (Calne, 1959), or when rupture leads to pneumoperitoneum (Somerville, 1951). Rarely, large intestinal pneumatosis is responsible for obstruction (Meikle, 1965), intussusception and volvulus (Burn and Jones, 1961). Such cystic pneumatosis is also known to occur in small bowel and again is usually benign (Hughes *et al.*, 1966).

In contrast, another variety of intramural gas is recognized, of different significance and gravity, and this is typified by the pneumatosis intestinalis of neonatal necrotizing enterocolitis. The aetiology of this condition remains obscure, but there is probably necrosis of the bowel wall followed by infection with gas-forming organisms (BMJ Editorial, 1978). The initial necrosis may be due to such factors as asphyxia, hypovolaemia, etc. The appearance of curvilinear streaks of intramural gas, as opposed to cystic gas, indicates a serious illness which frequently leads to intestinal perforation and a fatal outcome.

The present case bears many similarities to neonatal necrotizing enterocolitis both in aetiology (hypotension and hypoxia certainly occurred prior to the development of pneumatosis) and in clinical features, and we believe that it represents a form of necrotizing enteritis occurring in an adult as a post-operative complication. Such "serious" intramural small bowel gas has also been reported in adults in the epidemic infections known as "pig bel" (Murrell and Roth, 1963) and "darmbrand" (Fick and Wolken, 1949), as a complication of various collagen diseases (Kleinman *et al.*, 1976) and following frank infarction of bowel.

We use this case to suggest that a diagnosis of necrotizing enteritis should be added to the list of causes of post-operative collapse. Diagnosis may be made by a careful search for intramural gas on a plain abdominal film and, as with neonates, conservative treatment may be adequate providing there is no evidence of perforation.

REFERENCES

BMJ EDITORIAL, 1978. Necrotising enterocolitis. *British Medical Journal*, *i*, 132.

BURN, J. E. and JONES, B. S., 1961. Pneumatosis cystoides intestinalis, *British Medical Journal*, *ii*, 747–749.

CALNE, R. Y., 1959. Gas cysts of the large bowel simulating multiple polyposis. *British Journal of Surgery*, *47*, 212–215.

DENDY MOORE, H., 1968. Diagnosis and natural history of gas cysts of the colon, *British Medical Journal*, *ii*, 536–537.

FICK, K. A. and WOLKEN, A. P., 1949. Necrotic jejunitis. *Lancet*, *256*, 519–521.

HUGHES, D. T. D., GORDON, K. C. D., SWANN, J. C. and BOLT, G. L., 1966. Pneumatosis cystoides intestinalis. *Gut*, *7*, 553–557.

KLEINMAN, P., MEYERS, M. A., ABBOTT, G. and KAZAM, E., 1976. Necrotising enterocolitis with pneumatosis intestinalis in systemic lupus erythematosus and polyarteritis. *Radiology*, *121*, 595–598.

MARSHAK, R. H., BLUM, S. D., and EL'ASOPH, J., 1956. Pneumatosis involving the left side of the colon. *Journal of the American Medical Association*, *161*, 1626–1628.

MEIKLE, G., 1965. A case of pneumatosis coli. *Journal of the Royal College of Surgeons of Edinburgh*, *11*, 65–67.

MURRELL, T. G. C. and ROTH, L., 1963. Necrotising jejunitis: a newly discovered disease in the Highlands of New Guinea. *Medical Journal of Australia*, *3*, 61–69.

SOMERVILLE, P., 1951. Gas cysts of the intestine with pneumoperitoneum. *Lancet*, *261*, 1160–1161.

1981, *British Journal of Radiology*, *54*, 268

Case reports

The ultrasound diagnosis of hydatidiform mole and coexistent fetus associated with elevated maternal serum alpha feto protein

By G. H. R. Lamb, M.B., Ch.B., F.R.C.R. and *R. Oakley, M.B., Ch.B., D.M.R.D.

Department of Ultrasound, Mill Road Maternity Hospital, Liverpool L6 2AH

(*Received July 1980 and in revised form October 1980*)

CASE REPORTS

Case 1

A 36-year-old primigravida was seen in the antenatal clinic. At this stage gestation was ten weeks by dates but the uterus was slightly larger on examination. Four weeks later the patient was found to be hypertensive (BP 180/120) and had experienced persistent vomiting for two weeks. On ultrasound scan a large placenta containing vesicles was demonstrated, and, lying low down in the uterus, a viable fetus of approximately 15 weeks gestation was visible. The maternal serum α feto protein level (AFP) at this stage was 164 μg/l (normal median value at 15 weeks 31 μg/l Median × 2.5 78 μg/l. Liverpool University). In view of these findings the patient was admitted for termination. Post mortem revealed a 15-week fetus with a large spina bifida defect. The placenta showed hydropic changes consistent with hydatidiform mole.

Case 2

A 32-year-old gravida 5 para 4 patient was examined in the antenatal clinic. The uterus was 24 weeks by size and the patient had hypertension BP 170/110 and pre eclampsia. On ultrasound examination the uterus was almost entirely filled with placental tissue which contained numerous cystic spaces. A viable fetus was visible and thought to be about 15-weeks by size. Maternal serum α feto protein level at this time was 279 μg/l within the normal range for 24 weeks gestation but elevated for 15 weeks gestation. At termination the placenta showed changes consistent with hydatidiform mole and an apparently normal fetus, crown–rump length 11 cm, equivalent to 17–18 weeks.

DISCUSSION

The incidence of hydatidiform mole has been variously reported to be between 1 in 2000 and 1 in 2500 (Novac and Woodruff, 1974). The incidence of hydatidiform mole and coexistent fetus is even rarer and has been estimated to occur in between 1 in 10000 and 1 in 100000 pregnancies (Cunningham *et al.*, 1977).

The diagnosis of hydatidiform mole and coexistent fetus may be unsuspected clinically and even though ultrasound is a reliable technique for the diagnosis of hydatidiform mole (Ballas *et al.*, 1977) there may be doubt as to the abnormality of the placenta when a living fetus is also present.

The two patients described in this article were referred for ultrasound because of hyperemesis in Case 1 and hypertension in Case 2. However, both had had routine maternal serum α feto protein estimations and these were found to be abnormally high. In Case 1 there was an abnormal fetus with spina bifida but in the second case no such abnormality was present. This represents the second case of an association between raised maternal AFP and the diagnosis of hydatidiform mole and coexistent fetus. A previous report (Smith *et al.*, 1980) described a similar association. It would seem that this association, although rare, needs to be added to the other causes of a raised AFP, namely twins, threatened abortion and some congenital abnormalities of the gastrointestinal tract (Clark *et al.*, 1977), and emphasises the need for careful ultrasound examination of the placenta as well as the fetus in patients with a raised AFP.

REFERENCES

Ballas, S., Peyser, M. R. and Toaff, R., 1977. Diagnosis of hydatidiform mole with and without coexistent fetus by non-stored image echography. *Obstetrics and Gynecology*, 50, 182–185.

Clarke, P. C., Gordon, Y. B., Kital, M. J., Chard, T. and McNeal, A. D., 1977. Alpha feto protein levels in pregnancies complicated by gastrointestinal abnormalities of the foetus. *British Journal of Obstetrics and Gynaecology*, *84*, 285–289.

Cunningham, M. C., Walls, W. J. and Burke, M. F., 1977. Grey scale ultrasonography in the diagnosis of hydatidiform mole with a coexistent foetus. *British Journal of Obstetrics and Gynaecology*, *84*, 73–75.

Novac, E. and Woodruff, J. D., 1974. *Novac's Gynaecologic and Obstetric Pathology*, 7th Edit. (W. B. Saunders, Philadelphia).

Smith, D. H., Picker, R. H., Saunders, N. D., Sinosich, M. and Grudzinskas, J. G., 1980. Hydatidiform mole with coexistent viable foetus detected by routine AFP screening. *British Medical Journal*, 1213.

---

*Present address: Royal Liverpool Hospital, Prescot Street, Liverpool L3.

1981, *British Journal of Radiology*, *54*, 269–270 MARCH 1981

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Use of diagnostic ultrasound to measure the lumbar spine canal

THE EDITOR—SIR,

We support Drs. Stockdale's and Finlay's remarks (1980) concerning the use of ultrasound in the study of the lumbar spine.

In our experience quite accurate measurements of the AP diameter of the lumbar neurocanal are possible by means of ultrasound (Fig. 1A). We have, however, failed to obtain any other valuable information as to geography of the neurocanal or condition of the surrounding structures. In the particular instance of stenosis of the lumbar spine ultrasound fails to give any information on the presence or not of narrowing of the lateral recesses and general shape of the canal. These two parameters together with the actual AP diameter of the canal are essential for proper medical or surgical management.

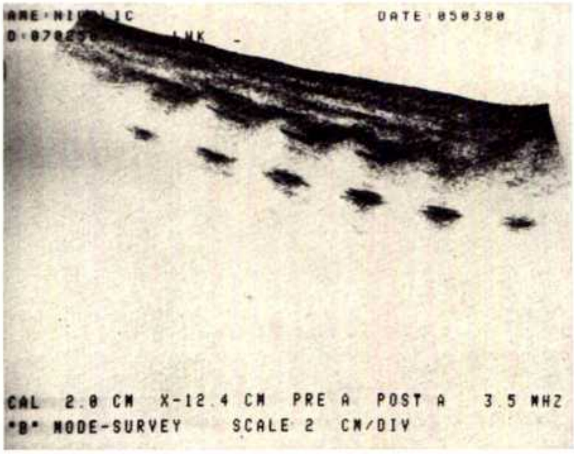

DATE 050380
CAL 2.0 CM X-12.4 CM PRE A POST A 3.5 MHZ
"B" MODE-SURVEY SCALE 2 CM/DIV

FIG. 1A.

Ultrasound image of lumbar spine showing a reduced AP diameter of 12.4 cm (16.0 cm normal) at level of L3 confirmed at operation.

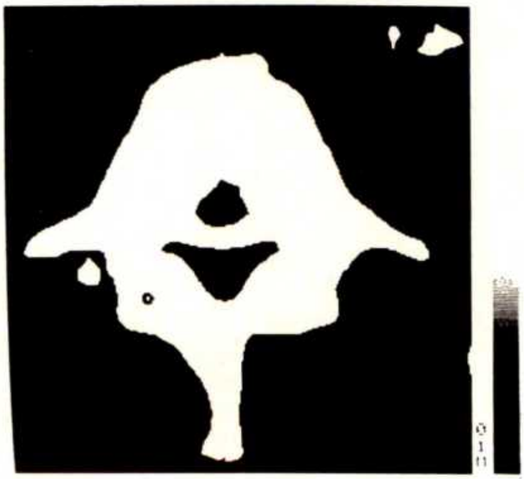


FIG. 1B.

CT scan of lumbar spine of another patient at level of L3. Unlike ultrasound image of Fig. 1A cross section of neurocanal with narrowing of lateral recesses is demonstrated. AP diameter also 12.4 cm, but incremental information was obtained.

It is our conviction that in the study of the lumbar spine CT scanning excels over conventional radiography and ultrasound (Fig. 1B).

Yours, etc.
J. A. VEIGA-PIRES,
R. V. D. BEEK,
M. C. KAISER.

Department of Radiology,
University Hospital (AZU),
PO Box 16250
3500 CG Utrecht, Netherlands.
(*Received November 1980*)

REFERENCE

STOCKDALE, H. R. and FINLAY, D., 1980. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *53*, 1101–1102.

(*Authors' reply*)

Use of diagnostic ultrasound to measure the lumbar spine canal

THE EDITOR—SIR,

We welcome the comments made by Dr. Veiga-Pires and his colleagues on the subject of ultrasound measurements of the lumbar spine. However, we are not in a position to support their views on the use of ultrasound to quantify the AP dimension of the neurocanal. We can very occasionally produce acceptable "B" scan images of the spinal canal in children and young adults when an abdominal scan is being performed.

We fully endorse their comments that CT scanning is to be preferred to either conventional radiography or ultrasound when one wishes more accurately to observe the canal shape.

Yours, etc.
H. R. STOCKDALE,

Medical Physics Department,
City Hospital,
Hucknall Road,
Nottingham NG5 1PD.

D. FINLAY.

X-ray Department,
University Hospital,
Queen's Medical Centre,
Nottingham NG2 7UH.
(*Received December 1980*)

Gold grain dosimetry

THE EDITOR—SIR,

The letter from Gibb and Massey (1980) will be widely welcomed by all users of the Manchester system of radium dosage.

However I am somewhat concerned that the choice of ^{198}Au as an example of a short lived radium substitute may lead to some confusion in the minds of people who have been using the Radiochemical Centre (TRC) Technical Bulletins 69/6 and 71/7 for guidance. These suggest that although the absorbed doses after total decay from 4.9 mCi of ^{198}Au and 1.0 mCi of radon are the same, an allowance of about 10% should be made because the biological effect of the gold is greater owing to its shorter half life. This leads to a value of 4.5 mCi of ^{198}Au being equivalent to 1.0 mCi of radon, or to a permanent implant of 34 mCi being equivalent to 1000 mg hours of radium dosage delivered over seven days, radon being assumed to be biologically equivalent to radium.

The consequence of this is that when the dose from a gold grain implant is calculated according to TRC Bulletins the dose actually delivered is 10% lower than the prescribed dose although biologically equivalent to the prescribed dose delivered by radon. It follows that where users of gold grains who have been calculating their doses according to the advice in TRC Bulletins wish to change to the data given in Gibb and Massey's letter, the prescribed dose should be reduced by 10%.

Yours, etc.
C. BINKS.

Medical Physics Department,
St. Luke's Hospital,
Guildford, Surrey GU1 3NT.
(*Received December 1980*)

REFERENCE

GIBB, R. and MASSEY, J. B., 1980 Radium dosage: SI units and the Manchester system. *British Journal of Radiology*, *53*, 1100–1101.

Book reviews

The Narrow Lumbar Canal. Radiologic Signs and Surgery. Ed. A. Wackenheim and E. Babin. pp. xiii+170, 139 figs, 1980 (Springer-Verlag, Berlin/Heidelberg/New York) DM168.
ISBN 3-540-09443-1

This is the printed version of a post-graduate course organized by the two editors in Strasbourg in 1979. The 28 contributors, mainly from France and the Benelux countries, included 17 neuro-radiologists, the others being neurologists, neuro- and orthopaedic surgeons.

Spinal stenosis has been one of those subjects tending to attract enthusiasts or repel sceptics and has only recently gained respectability as a recognized clinical entity. The subject has always been confusing because of the fact that functional stenosis can occur as a consequence of alterations in cross sectional shape of the canal and that diagnosis could not always be made by measurements alone. The recognition of morphologic changes in the canal on plain films had already been elucidated when computed tomography arrived to prove the point in a very dramatic way.

In this book, the emphasis is on the recognition of lumbar stenosis, mainly by conventional radiographic techniques *i.e.* plain radiography, gas and positive contrast myelography and radiculography. A chapter on CT scanning is contributed by a team from Brussels and the value or otherwise of spinal venography is discussed by contributors from Strasbourg, Santander and Caen.

Some of the aspects of spinal stenosis are contentious and the reviewer was pleased that, early in the discussion, Roulleau and Guillaume counselled against relying too heavily upon drawing lines and making measurements on films. He did object however to such statements as "degenerative spondylolisthesis secondary to osteoarthrosis of the apophyseal joints is always fixed on flexion/extension films". (Chap. 10 P.93 figs. 91 and 92). This is quite untrue and could be very misleading to a beginner.

On the subject of spondylolisthesis, in chapter I, pars interarticularis defects are described as developmental and no reference whatever is made to Newman's Classification in which he states that the isthmic defects, occurring in 5% of the population, are almost always fatigue fractures.

However, these are perhaps small points in the total subject and do not detract from the value of the book as a whole which gives a good introduction to anyone approaching the subject; the wealth of illustrations are for the most part excellent (a standard we now take for granted in Springer-Verlag Publications), and there is a good bibliography.

J. T. PATTON.

Atlas of Lymphography. By M. Viamonte and A. Rüttimann, pp. xi+456, 1980 (Georg Thieme, Verlag Stuttgart), DM.198.
ISBN 3-13-5478-01-7

This book is edited by two of the best-known names in lymphography with contributions by other authors well-known in this field. It sets out to be an atlas of lymphography and in this it succeeds brilliantly. This book is profusely illustrated, the illustrations are excellent and they make their point.

The atlas starts with an excellent chapter on histology, anatomy and lymphographic appearance, which answers succinctly many of those questions which one is often asked by radiologists in training and one's clinical colleagues. One can always find points to criticise, which means points on which the authors' and the reviewer's opinions and prejudices differ. I would contend that it is more comfortable for the patient for the marker dye to be injected below the skin above the interdigital space as opposed to into the interdigital space. In the section on anatomy, which is very detailed, the echelon nodes in the drainage of the testis are not mentioned, although they are mentioned in passing in a later chapter, but this sort of information is vital when guiding one's radiotherapeutic colleagues. Also, on p. 117, pulmonary oil embolism is mentioned as a severe complication. This must be a mistake because pulmonary oil embolism occurs in pretty well every case in which a diagnostic amount of contrast medium is given and this should be differentiated from lipiodal pneumonia. Reading a statement like this could cause alarm to those not well versed in lymphography, particularly if they took low kV chest films following lymphography.

In Chapter 8, I would contend that the evidence is that carcinoma of the prostate can involve the nodes long before there is any haematogenous spread and therefore lymphography is not positive only late in the disease. However, the stress laid on the involvement of the para-aortic nodes in carcinoma of the cervix and body of the uterus is very important, since this is not widely realised and many deaths could be prevented by lymphography and adequate treatment in these patients.

I assess this as an excellent book and of great value to any department using lymphography.

J. S. MACDONALD.

Forthcoming events

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Radiographic Systems: What is Best?

British Institute of Radiology all-day meeting on Wednesday, March 18, 1981 at 32 Welbeck Street, London W1M 7PG, starting at 10.00. Chairmen: Dr. M. J. Day and Dr. J. H. E. Carmichael. Other speakers: Dr. J. Roylance, Miss R. E. Stapleton, Mr. G. Waters, Dr. B. M. Moores, Dr. G. M. Ardran, Dr. D. H. Trapnell and Dr. E. Robertson. Enquiries to General Secretary.

Ethical and Legal Aspects of Radiological Protection

Imperial College, London, Tuesday, March 31, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, DD1 4HN.

Spring Meeting, BIR/RCR/RSM

A joint Spring Meeting, organized by the Royal College of Radiologists, will be held in Bristol on April 3–4, 1981. For further information contact the General Secretary, the Royal College of Radiologists, 38 Portland Place, London W1.

BIR Annual Congress 1981 and Scientific Exhibition

The British Institute of Radiology Annual Congress will be held on April 9–10, 1981 at the Royal Free Hospital and will include the Mackenzie Davidson Memorial Lecture by R. G. Grainger on "Intravascular contrast media—present perspectives". Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

BIR Annual Dinner

Thursday, April 9, 1981, at Lord's Banqueting Centre, London NW8. Enquiries and tickets, General Secretary, 32 Welbeck Street, London W1M 7PG.

Physics in Medical Ultrasound
Durham, April 13–14, 1981

This meeting, organized by the HPA Ultrasonics Topic Group in association with the British Medical Ultrasound Society, is intended to provide a forum for the presentation and discussion of scientific and technical aspects of ultrasound in medicine, and will be accompanied by an exhibition of commercial test and research equipment. Accommodation available. Information: Dr. T. A. Whittingham, Regional Medical Physics Department, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE.

Echocardiography

A course in Echocardiography will be held at Harefield Hospital from April 27 to May 1, 1981. The course is intended for those having experience in cardiac ultrasound and working in the field. Accommodation available. Further details from Mrs. M. Beech, telephone Harefield 3737, ext. 609.

BIR Meetings, May 1981

Thursday, May 14: State of the Art Seminar on Preparation of the Bowel Prior to Radiology (Chairman, Dr. G. J. de Lacey) at 17.45; and Radiology of the Colon (speakers to include Drs. C. Bartram and C. Williams) at 19.40. Friday, May 22: Radiobiology work-in-progress meeting on Hyperthermia, at 11.00.

British Association of Clinical Anatomists

The summer meeting will take place in the Teaching Centre of the Norfolk and Norwich Hospital on Friday, May 8, 1981. During the meeting, at 4.30 p.m., Dr. D. H. Woollam will give the Arris and Gale lecture on "The circumventricular organs: their role as possible sites for neurosurgery".

Further details about the Association may be obtained from the Secretary, Professor D. B. Moffat, Department of Anatomy, University College, PO Box 78, Cardiff CF1 1XL.

Annual General Meeting

The Annual General Meeting of the Institute will be held on Thursday, May 14, 1981. All members will receive notification.

Fourth European Congress on Ultrasonics in Medicine

This will be held in Dubrovnik, May 17–24, 1981, sponsored by EFSUMB and organized by the Yugoslav Association of Societies for Ultrasound in Medicine and Biology. Information from Dr. Višnja Latin, M.D., D.Sc., President of the Organizing Committee, Jagode Truhelke, 26, 41090 Zagreb, Yugoslavia.

Fifth Congress of the European Nuclear Medicine Society
Nineteenth Congress of the Societa Italiana di Biologia e Medicina Nucleare

Pisa, June 9–12, 1981. Main suggested topics: cardiovascular applications of radionuclides *in vivo* and *in vitro*; advances in regional lung morphofunctional studies; development of radioimmunoassay in comparison with non-radioactive immunochemical techniques; advances in nuclear imaging in comparison with alternative techniques. Official language: English. There will also be an industrial and technical exhibition.

Registration forms and other information from: The Organizing Secretariat, OIC, Via G. Modena 19, 50121 Florence, Italy. (Registration by April 15, 1981).

Radiology of the Small Intestine

A one-day course will be held on Wednesday, June 17, 1981 at the John Radcliffe Hospital, Oxford. Registration fee £21·00. For further details contact: Dr. D. J. Nolan, Department of Radiology, John Radcliffe Hospital, Oxford OX3 9DU (phone (0865) 817238).

Second International Congress on the Ultrasonic Examination of the Breast

Institution of Electrical Engineers, Savoy Place, London, June 22–23, 1981. Further details available from Dr. J. C. Bamber, Block F, Institute of Cancer Research, Clifton Avenue, Sutton, Surrey SM2 5PX.

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Programme from: ICR81, c/o Brussels International Trade Fair, Parc des Expositions B-1020, Brussels, Belgium.

Forthcoming events

First International Symposium on Minimal Invasive Cancer

Organized by the University Clinic of Obstetrics and Gynaecology, Graz, Austria, to be held at the Kongresshaus, Graz, July 1–4, 1981. Language: English. Main topics: cervix, vulva, endometrium, breast, oesophagus, stomach, large intestine, lung, thyroid, urinary bladder, prostate, larynx, oral cavity, skin, other organs. Enquiries: Interconvention, PO Box 105, A-1014, Vienna, Austria (phone (0222) 57 62 88). President: Prof. E. Burghardt; Secretary General, Dr. E. Holzer.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

Prospective Methods of Radiation Therapy in Developing Countries

The International Atomic Energy Agency will hold a seminar in Kyoto, Japan, August 31–September 4, 1981, intended for senior radiobiologists and/or medical doctors. The main objects are to review and discuss possible physical chemical and biological methods to improve the results of radiation therapy comparable to high LET radiation, and to stimulate research. Working language: English.

Information from D. A. Herbert, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4QJ. Applications and abstracts by March 15.

Radionuclides in Nephrology
Fifth International Symposium

September 2–4, 1981, at The Royal Society, London. Further details from A. R. Constable, Institute of Urology, 172 Shaftesbury Avenue, London WC2 8JE. Closing date for abstracts April 20.

European Association of Radiology
II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

Radiology of the Mediastinum
4th Postgraduate Course in Radiology "P. Perona"

Will be held in Verona, Italy, October 1–3, 1981, organized by the Institute of Radiology of the University of Verona, the Italian Society of Radiology, and the College d'Enseignement Post-Universitaire en Radiologie. Simultaneous English/French translation. Registration L.65000. Information: Radiology Department, University Hospital, Verona (phone 045/582445).

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

Symposium on Education and Training in Radiobiology

Dresden, May 12–15, 1982. Organized by the Gesellschaft für medizinische Radiologie der DDR, under the auspices of the European Society of Radiology. Languages: English, French and German. Registration by December 1, 1981; papers by August 15, 1981. Information: Professor R. Barke, Radiologische Klinik, DDR – 8019, Dresden, Fetscherstrasse 74.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01-486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

Book reviews

UV-A Biological Effects of Ultraviolet Radiation. By J. A. Parrish, R. R. Anderson, F. Urbach and D. Pitts, pp. ix+262, 1978. (John Wiley, Chichester/New York), £15·00.
ISBN 0-471-99759-5

It was rather a surprise to find a book of this title. The preface tells how it came to be written, out of regulatory politics and the use of UVR for resin polymerization of dental fillings. There is no mention of fears about photochemotherapy with psoralens for psoriasis, so-called PUVA, playing a part.

The important function this book fulfils is to emphasize how little we know about the action of near ultraviolet, so-called UV-A (315–400 nm), on living systems. A rather unkind colleague remarked that the essential information on the biological effects of UV-A could be written on the back of a postcard, the really vital on the back of a postage stamp. This is of course an exaggeration, so, to give it more body, the book is filled out with information on the adjoining spectrum, about better established effects.

Now to a closer look at individual chapters. Chapter one is a general elementary introduction on the electromagnetic spectrum and overall is clear and satisfactory except that I was sorry to see that the spectral limits defined for UV-A, UV-B and UV-C are not those laid down by the Commission Internationale d'Éclairage (CIE).

Perhaps paradoxically, the CIE is faithfully observed with respect to radiometric symbols in Table 2.1 of Chapter 2, which is an accurate account of UVR sources, etc; the sections on solar UVR are clearly written, those on filters and other optical equipment particularly useful.

Chapter three on UV radiometry is again clear and accurate; an appendix on manufacturers of equipment gives postal addresses, but for the North American only. Chapter four deals well with optical properties of the skin, and it is good to see that the pioneering conceptions of George Findlay receive their belated recognition.

Chapter five is a relatively brief review of the action of UVR, mostly longwave, on bacteria; Chapter six deals at greater length with these effects in normal skin; both topics are well managed. The latter chapter has a number of useful summarizing tables. There is current interest in the additive effects of various parts of the spectrum, *viz.* so-called "photoaugmentation". However, there seems to be a misinterpretation on page 124. This is on the phenomenon of "photorecovery" of skin erythema from UVR, *i.e.* the lessening of the response by subsequent exposure to longer wavelength radiation. The authors state that the extent of photorecovery, 20–40%, is within the error of determining the minimal skin erythema dose. This remark contains the tacit verdict that photorecovery is probably not real. But the workers referred to, van der Leun and Stoop (1969), had in fact tested their results statistically; my understanding of the work is that the extent of photorecovery was modest, but probably real. Since this book went to press, more recent work by van Weelden has shown that photorecovery is undoubtedly real.

Chapter seven deals with the adverse effects of light on skin. The approach is sound enough and orthodox; some of us would favour that the obfuscating dogma of "photoallergy" and "photo-toxicity" should be rehearsed slightly more critically.

Chapter eight is a good survey of carcinogenesis by UVR with a balanced account of the more recent epidemiological developments but without much on UV-A.

Chapter nine, on the effects of UVR in the eye, starts with several useful pages of anatomy and physiology before reviewing the spectral researches of Pitts and others; it includes some unpublished data. Chapter ten reviews PUVA treatment; this is reasoned and restrained and I welcome the absence of sales pressure extolling it or doomwatch pessimism condemning it. Chapter 11 deals with safety measures largely relying on the work and suggestions of Dr. David Sliney and accepted by NIOSH (The National Institute for Occupational Safety and Health). These standards are widely used though some consider them unnecessarily restrictive and one hears them criticized for not being suitable for application to skin. Nevertheless they constitute a start for developing sensible measures for UVR safety.

Perhaps in a way this book is slightly before its time; the title is a little misleading. If the publishers had waited another year or so, there would perhaps have been more to write about on UV-A. But one is quite content to have this book as it is. It is obviously very useful to all medical physicists and photobiologists; they should have it or access to it.

I. A. MAGNUS.

Handbuch der medizinischen Radiologie. Teil 1A Nuklearmedizin. Eds. L. Diethelm *et al.*, 244 figs., 65 tables, pp. 722 1980 (Springer-Verlag, Berlin), DM. 540, £126.
ISBN 3-540-08487-8

This book is the first of a four-part volume dealing with all aspects of nuclear medicine. Its main sections deal with radiopharmaceuticals, the production of radioisotopes, basic principles of the measuring of ionizing radiation, gamma cameras, neutron activation analysis, data processing and a large section dealing with all aspects of radiation protection. Three sections are written in English, and the remainder in German. There are two subject indices; one in German with English translations and one in English with German translations. These are comprehensive and good enough to be useful as vocabularies.

The various sections have been written by 20 authors. As a result some chapters are well written and lucid, whereas the style and clarity of other chapters leave something to be desired. This fluctuation diminishes the reader's satisfaction, and this is disappointing because a great deal of devoted effort has been made in publishing this well-printed and attractively-bound volume.

The publication of this volume raises the whole question of the value of medical encyclopedias. In the past they have served to fill the gaps in detail and history which standard textbooks had omitted and were particularly valuable in the more static disciplines. However, nuclear medicine is expanding and seems likely to do so for the foreseeable future. This expansion has contributed, no doubt, to the vogue for congresses and symposia and to the enthusiasm there is for journals of rapid communication. Thus, encyclopedias will be outdated even at the time of publication. For example, the use of DMSA is regarded as experimental, and *in vivo* ^{99}Tc^{m}-labelling of red cells is not mentioned, although both these preparations are already in widespread daily use. In day-to-day work it is the custom to rely more on monographs, and original published work, and less on textbooks and encyclopedias.

The value of an encyclopedia as a book of reference and historical record is less questionable. Alas, the present volume falls between two stools. Occasionally the mathematical manipulations are so complicated as to be beyond a mere clinician but in other places inadequate for the scientist who genuinely wants to come to terms with the developments and arguments of a new discipline. As a book of reference it does not offer a way of addressing important questions arising from the daily clinical work. In general, the impression is unavoidable that the bulk of the book has been compiled by scientists and engineers, and its main themes are directed to these professions. And yet the main attractions of a book of this kind should be to clinicians.

The volume is a well-executed earnest of considerable endeavour, but in a discipline where it requires considerable effort to keep abreast of developments it seems an anachronism The reviewers are drawn reluctantly to the conclusion there will be little clinical incentive to read it.

H. F. FREUNDLICH,
E. RHYS DAVIES.

Screening in Cancer: A Report of a UICC International Workshop, Toronto, Canada, April 1978, pp. 338, 1979 (UICC Technical Report Series—Volume 40) (UICC, Geneva), Sw. fr. 20.

The notion of pre-symptomatic screening for signs of incipient chronic disease or its detectable precursors is far from new. Much of the routine of general physical examination (especially the standard tests of urine and other accessible fluid) represents non-specific screening, since it does not derive directly from the need to investigate the cause of the presenting symptoms. In paediatric and obstetric practice the systematic examination of well persons for possible early signs of ill health has been routinely accepted for many years and the general "check up" is well established in countries where doctors expect to be paid directly by those they examine or advise. What is relatively new is the proposal that whole adult populations should be subjected to systematic and repeated examination for the early signs of serious illness, with a view to the institution of an earlier intervention in respect of those detected as ill than could be hoped for if reliance was placed on each patient recognizing the symptoms of the condition and initiating a consultation.

Although such pre-symptomatic screening might be feasible in relation to quite a wide range of chronic diseases it has emerged as a serious issue largely in relation to cancer and so far mainly in relation to cancer of the uterine cervix, breast, lung, stomach and large bowel. The present volume is a useful review of the present possibilities in relation to these conditions and presents some helpful discussion of the advantages and disadvantages.

A preliminary consideration of the subject might conclude that there can only be advantages since conventional wisdom endorses the value of early diagnosis as a means of improving prognosis. As this volume makes fairly plain, such a conclusion would be distinctly premature. Screening by the use of presently available techniques in the light of present knowledge and understanding of the disease processes involved is distinctly problematic. In no case is there unequivocal evidence of benefit and there is remarkably little data available on costs.

For a screening procedure to be acceptable for general application to the community it must be reliable in detecting the relevant disease process; it must result in a more successful treatment than is available when the disease is diagnosed following the presentation of symptoms; it must result in substantially less hazard to health than would be involved in waiting for symptoms to appear; it must be acceptable enough to the population to ensure that it is applied to most of those likely to benefit; and it must represent a reasonable use of the required resources in the sense that the gains would be commensurate with those to be derived from alternative resource deployments.

The evidence is that no pre-symptomatic test for early cancer or its precursors has yet come near to satisfying these evaluative criteria. The procedure with the best credentials at present is cytological screening for carcinoma *in situ* of the cervix and this has only recently been applied in any community on a scale sufficient to be capable of demonstrating benefit. Benefits from other procedures have yet to be demonstrated—partly because of methodological difficulties and partly because the procedures have yet to be introduced systematically on an adequate scale. Costs remain largely unspecified and certainly unquantified except in the simple sense of the financial implications of the actual screening service. Social costs—particularly relevant in some screening procedures which can arouse substantial anxiety—have scarcely begun to be assessed and medical costs in terms of morbidity arising from the screening procedures or consequent further investigation have not been adequately quantified.

The present volume is encouraging to the extent that it demonstrates the considerable interest that is current as well as the volume of thoughtful and well-designed investigation now underway. Unfortunately the editing of what is a collection of disparate essays leaves a considerable amount of repetition. Nevertheless the work as a whole is valuable and easy to read or consult.

A. SMITH.

Screening for Cancer. Theory, Analysis and Design. By D. M. Eddy, pp. xii+308, 1970 (Prentice-Hall International, Hemel Hempstead), £19·45.
ISBN 0-13-796789-6.

The purpose of this book is to describe a theory of screening and its applications in screening for five malignant diseases, as well as the design of a specific cancer screening programme. The work is aimed at all people involved with screening—clinicians, administrators, health planners, statisticians and epidemiologists. The author has succeeded in writing a work that will be of interest to all such collaborators.

The mathematical content has been purposely limited but is still considerable, although some mathematical concepts have been simplified by conversion to geometrical illustrations. Some sections are written for individuals with special interests *e.g.* "Sensitivity of mammography at the initial screening session", "Constructing a mortality function" and "Radiation hazards". These sections are clearly marked and may be omitted by others without a break in the continuity of the work. In addition, the important concepts and results in difficult chapters are summarized in separate sections. This reviewer took the easy option in by-passing the mathematical sections and in accepting the conclusions "on faith".

The book is mainly devoted to a mathematical model for breast cancer screening. The adaptation of this theory to screening for malignancies of the cervix, lung, bladder and colon is also discussed more briefly. The problems and results of screening programmes are discussed fairly and policy recommendations are made on the basis of medical cost-effectiveness and administrative feasibility.

The efficacy of screening for detection of disease is still controversial. This book will stimulate discussion and debate. It is recommended to all interested parties.

I. H. GRAVELLE.

Radiology of Haemophilic Arthropathies. By J. Forrai, pp. 145, 1979 (Martinus Nijhoff, The Hague), Guilders 50.
ISBN 90-247-2130X.

This book has 75 figures, many of them containing more than one illustration. They are of good quality, and all but one concern the skeletal system. The text is brief, and the bibliography comprehensive up to the date of publication. However, the references are published sequentially as they appear in the text. An alphabetical presentation might have been more helpful. The brief text covers the subject adequately, so far as radiological appearances are concerned.

However, a book on so small a subject is essentially a monograph and in medical practice in this country it is often considered that a monograph should be more comprehensive and cover a wider spectrum of knowledge and data. It can be said that the data in this book are accurate as far as they go, and the illustrations are good.

J. H. MIDDLEMISS.

Book reviews

Encyclopaedia of Medical Radiology. Vol 5. Part 6. Bone Tumours. Edited by K. Ranniger, pp. xix+825, 1977 (Springer-Verlag, Berlin/Heidelberg/New York), DM 370, $162.80.

Bone tumours have always exercised a fascination for radiologists (not to mention pathologists), which increases the further one becomes involved in bone disease, and such fascination is totally out of proportion to the importance of the subject in everyday bone radiology. Most radiologists have a rough idea that an adamantinoma of a long bone is a curiosity that usually occurs in the tibia, yet how often does one meet the entity in a working lifetime? In contrast, most radiologists are looking at McNab's traction spurs most days of their lives, yet how many recognize them for what they are? They somehow do not possess the drama of a tumour.

For those who like bone tumours—and there is no doubt that there is great satisfaction in getting these rare lesions right—here is the book which will keep their eyes down for many hours. It is one of the series "Encyclopaedia of Medical Radiology" published by Springer with seven chief editors, all of whom are from Germany. The bone volume is under the overall editorship of Friedrich Heuck of Stuttgart but the text, with the exception of the first seven pages by Professor Schajowicz of World Health Organization, is entirely by North American authors. This is quite proper as there is no doubt that this is where the greatest expertise lies, both in diagnosis and treatment.

American doctors do not appear to be so proscribed by demarcation rules as in the U.K. and radiologists are prepared to involve themselves in the pathological and clinical aspects rather more than their British counterparts. They are thus able to speak with much more confidence and this authority shines out of the chapters, for example, by Frieda Feldman on chondroid tumours and Melvin Becker and his co-authors on tumour-like lesions. This broad approach is particularly important in bone tumours, where frequently there are differing views between radiologists and pathologists in terminology and classification of tumours.

The book is a very valuable statement of current concepts of the majority of bone tumours although obviously it cannot claim to be totally comprehensive even in 700 pages. It is a book mainly for departmental libraries rather than individuals unless they happen to be particularly involved with bone disease, in which case they cannot really afford to be without it. Within the department it will be a valuable reference book and the chapter by George Greenfield on the radiographic approach to bone tumours should be required reading for all trainees.

References are extensive and very few unqualified statements are made, although I think Greenfield might have given us the key references to the controversial subject of osteocytic bone resorption rather than ducking it by the statement "Osteocytes have also been shown to have osteolytic properties". Such a bald statement does not give the uninitiated a clue to the recent controversy on this subject. Similarly, "Hyperaemia is said to facilitate osteolysis", a statement undoubtedly accepted by most radiologists, does require some defending (notably to pathologists), particularly in the face of osteoblastic metastases in diffuse skeletal haemangiomatosis (p. 318). I suppose it depends on the type of hyperaemia.

The final three chapters are devoted to investigation by radionuclides, angiography and high resolution techniques. I would have thought 40 pages devoted to angiography was generous, especially when one finds that the whole subject of fibro-sarcoma is demolished in three pages including pictures. In his introduction to this section Dr. Yaghmai concludes with the statement that "since primary malignant bone tumours are so serious and tragic and treatment frequently mutilating, any contribution toward confirming or disproving their presence should be of value provided, like arteriography, (it) causes little or no harm to the patient". Such a statement needs no further comment.

One must not however air one's personal prejudices, and minor criticism of this sort cannot detract from the authority of this book which is obviously now the current standard work on the radiology of this subject.

J. T. PATTON.

Bone Tumors. Diagnosis and Treatment. By Joseph M. Mirra. pp. xiv+629, 1980 (J. B. Lippincott, Harper and Row, London) £45·25.
ISBN 0-397-50428-4

This excellent book is an example of the philosophy that the diagnosis and treatment of bone tumours is undertaken best by a team of pathologists, radiologists and clinicians, that none of these should be so proud as to claim his part more important than the others' nor too humble to attempt to wander into the others' diagnostic territory. The pathologist must recognise that on looking at the radiograph he is seeing gross pathology which he ignores at his peril and that histology alone can be totally misleading unless looked at in the context of the gross lesion.

The principal author, Dr. Joseph Mirra, is a pathologist from the University of California, Los Angeles, and in the first chapter he tackles the essentials of pathological diagnosis, getting down to such fundamentals as the apparatus that a pathologist will require, and describes in detail such techniques as the imprinting of specimens. Subsequent chapters are based on a pathological classification and each tumour is discussed from its clinical presentation, radiological appearances as well as the gross and microscopic pathology. Epidemiological information is given in succinct diagrams with full references and the book provides all that is required for a clinical team embarking upon (or continuing) a bone tumour service.

The authors do not hesitate to digress into "Indian territory". The concept of osteo- and fibro-sarcomatous de-differentiation of chondrosarcoma is discussed as well as such topical subjects as malignant fibrous histiocytoma. Another aside, "Malignant chondroblastoma—does such an entity exist", produces a very closely argued discussion with references on the approach to surgery of chondroblastoma—an invaluable aid to a surgeon tackling his first such lesion.

There is a refreshing no-nonsense style about the book with messages well punched home. However this is not the work of an opinionated dogmatist and all statements are well qualified by references.

An essential book for all who are involved in bone tumours and an invaluable reference book for all those doctors who meet these lesions only occasionally.

J. T. PATTON.

Diagnostic Ultrasound: Physical Principles and Exercises. By Frederick W. Kremkau. pp. xi+211, 1980 (Grune and Stratton, New York), $19.50.
ISBN 0-8089-1233-X

This book, by a physicist, sets out to describe the basic physical principles underlying diagnostic ultrasound but specifically avoids complex physics. It is aimed at radiographers and clinicians with no previous training in medical physics. The book is based on the author's experience in running postgraduate teaching courses at the Bowman Gray School of Medicine.

Since "Diagnostic Ultrasonics: Principles and Use of Instruments" by W. N. McDicken became unavailable in the UK, there has been a continuing need for a book on the basic physical principles of ultrasound which has not been satisfied by any of the many recent publications from the U.S.A. Dr. Kremkau's book goes a long way to filling this need and he has certainly been successful in maintaining a high degree of simplicity in his text. At the end of each section there is a list of "exercises" which the reader can use to assess his understanding of that section. These unfortunately contribute to approximately one third of the total size of this book and I am a little doubtful of their value since they tend to be too simplistic. Indeed the whole style of the book's construction and the English usage are very American even to the inclusion of a multiple choice question concerning the value of the book in which all 16 choices are excessively complimentary!

The book includes a useful glossary in which the definitions are commendably brief and there are also appendices of equations, physics concepts, algebra and trigonometry, logarithms and decibels. This book will undoubtedly be of value not only to the novices but also to the more experienced operator who has difficulty in understanding the principles behind the production of ultrasound images.

H. B. Meire.

Pediatric Ultrasound. By J. O. Haller and M. Schneider. pp. xi+279, 1980 (Year Book Medical Publishers, Chicago/London) £33·25.
ISBN 0-8151-4107-6

This is a North American book devoted to paediatric ultrasound. It covers echography of the abdomen including the pelvis and the testes with a section on the use of ultrasound in diseases of the chest. Echocardiography and neonatal echoencephalography are not included. There are small sections on the pregnant uterus and renal transplants which are an obvious reflection of the regional differences in the definition of paediatric practice. These particular sections are a little superfluous as the problems described are covered in better detail elsewhere.

Any radiologist picking up this book will be immediately struck by the poor quality of reproduction. This is surprising in view of the usual quality of the excellent publishing house. The book does have three great strengths and these lie in the text. There is still at the moment a relative paucity of published references on paediatric ultrasonography and those being asked to perform echographic examinations on children, particularly if they have a moderate or limited paediatric practice, require help in two main areas. Firstly a clinical thumb-nail sketch of the categories of disorder found amongst the various organs and secondly how these manifest themselves echographically. The addition of snippets of practical information would be a further bonus. The authors have succeeded admirably in providing all three in their excellent text. There are of course the inevitable mistakes but hopefully these will act as a stimulus for further interest and publication in this "cinderella" specialty. Criticism is easier than craftsmanship and although I have been critical of this book I would have no hesitation in recommending a radiologist to delve into its pages to help with the echographic diagnosis of paediatric problems.

C. Metreweli.

Abdominal Ultrasound, Static and Dynamic Scanning. By H. H. Holm *et al.*, 2nd edit., pp. 274, 1980 (Munksgaard, Copenhagen), D.Kr.300,00.
ISBN 0-8391-4134-3

This is the second edition of Professor Holm's book which was originally published too soon after the introduction of grey scale images to permit their inclusion. The new edition contains the work of eight separate contributors, all of whom have worked in Professor Holm's department in Copenhagen.

The first chapter briefly reviews the history of abdominal scanning whilst the second chapter reviews the basic physics. Although this has been done *ad nauseam* elsewhere the physics section in this book is fairly simple and easily understood. The major virtue of the book is the excellent anatomical sections, which comprise labelled colour photographs of transverse and longitudinal cadaver sections in addition to black and white anatomical drawings with illustrative ultrasound scans.

The clinical content of the book covers all abdominal uses of ultrasound, including pregnancy, and whilst the content of the text is generally useful, particularly the descriptions of the scanning approaches to different organs, the clinical images are rather disappointing. The low amplitude echo information is invisible in many of the reproductions, many images are too small and others are severely blurred. These limitations restrict the value of the book as a reference work for operators who are well experienced in ultrasound, but the anatomy and examination technique sections will be immensely valuable to those approaching the subject for the first time.

H. B. Meire.

Guide Pratique d'Echographie Abdominale. By J. Taboury, pp. ix+146, 1979 (Masson, Paris).
ISBN 2-225-63822-5.

This book, which is in French, consists of 11 chapters, the first two dealing with the physics and techniques of ultrasound and the rest with the intra-abdominal organs, abdominal masses and obstetrics and gynaecology.

The initial chapters are written with clarity and give precise indications for the use of different transducers and techniques. The chapters on the abdominal organs are all set out in a similar pattern with preparation and positioning of the patient, the ultrasound mode best suited to that particular organ, the variety of cuts indicated, the normal and abnormal appearances and finally the indications and limitations of the technique. These sub-headings are richly illustrated by excellent diagrams, particularly those dealing with the variety of angles involved in ultrasound scanning. The ultrasound pictures, a few of which are of indifferent quality, are all accompanied by line drawings demonstrating the normal and abnormal anatomy. The text is fairly detailed without being over-descriptive, and the number of pathological conditions described is not exhaustive. Indeed, there is very little on abdominal masses in children and the authors admit that their chapter on gynaecology and obstetrics is only a basic outline. There is no attempt to correlate the ultrasound findings with any other imaging mode. There is a short bibliography of both the English and French literature at the back of the book.

For me, the illustrations with accompanying diagrams and the simplicity in explaining the ultrasound cuts make this a useful book for the beginner. I hope that one day it is translated.

J. C. Parker.

Book reviews

Science in action 202
Die Röntgenuntersuchung im Kidnesalter 220
A professional approach to radiology administration 220
Review of medical terminology 240
Nuclear medicine annual 1980 249
1980 Year book of nuclear medicine 249
The narrow lumbar canal 270
Atlas of lymphography 270
UV-A biological effects of ultraviolet radiation 273
Handbuch der medizinischen Radiologie. 1A. Nuklearmedizin 273
Screening in cancer: UICC international workshop 274
Screening for cancer: theory, analysis and design 274
Radiology of haemophilic arthropathies 274
Encyclopaedia of Medical Radiology. 5, 6. Bone tumors 275
Bone tumors. Diagnosis and treatment 276
Diagnostic ultrasound 276
Pediatric ultrasound 276
Abdominal ultrasound 276
Guide pratique d'echographie abdominale 276

Special offer

Back issues of The British Journal of Radiology

Any edition of the B.J.R. up to and including December 1977 which is still available.

50p per copy (issues prior to 1940 **Free** on payment of postage, up to 31st March 1981)

Available stock dates back to 1931 (not all months)
Complete years: 1936, 1949, 1955, 1958, 1965, 1966, 1967, 1969, 1970, 1975 and 1976.

Enquiries:
British Institute of Radiology,
32 Welbeck Street, London W1M 7PG
01-935 6237/6867
All Journals subject to availability on receipt of order

VOL 54 NO 639 MARCH 1981

The British Journal of Radiology

Contents

Page

Radiation hazards: 25 years of collaborative research. Sylvanus Thompson Memorial Lecture, April 1980. 179
R. Doll

Mortality from cancer and all causes among British radiologists. 187
P. G. Smith and R. Doll

Clinical relevance of radiological abnormalities of the craniovertebral junction. 195
E. H. Burrows

Amipaque in coronary angiography and left ventriculography. 203
D. C. Cumberland

Radionuclide uptake during the evolution of experimental acute osteomyelitis. 207
S. H. Norris and I. Watt

Mammographic practice and dosimetry in Britain. 212
M. Fitzgerald, D. R. White, E. White and J. Young

Evaluating performance characteristics in computerized tomography. 221
D. R. White, R. D. Speller and P. M. Taylor

A survey of 29 EMI CT machines in Britain. 232
R. D. Speller, D. R. White, R. Veerappan, A. J. Coleman and P. E. Waller

Hydatid disease: the value of whole-body screening by scintigraphy with technetium-99m-labelled red blood cells. 241
D. Front and Ora Israel

Effect of hyperthermia on the hypoxic fraction in an experimental mammary carcinoma *in vivo*. 245
Jens Overgaard

Effect of X irradiation on the rectum of the rat. 250
F.-H. Hubmann

Technical notes. 255
  A phantom for assessing the resolution at depth of a gamma camera system.
    F. C. Gillespie
  Personalized fixation using a vacuum consolidation technique.
    C. W. Dickens

Case reports. 259
  Iodine 131 ablation therapy for a patient on maintenance haemodialysis.
    N. Howard and M. Glasser
  Intermittent cyanotic attacks on an infant—an unusual presentation of a congenital anterior diaphragmatic (Morgani) hernia.
    M. D. Cohen
  A calcified renal mass: chondrosarcoma of kidney.
    J. Pitfield, B. J. Preston and P. G. Smith
  Computed tomography in diabetes insipidus: posterior empty sella.
    G. D. Marano, J. A. Horton and A. M. Vazquez
  Pneumatosis intestinalis in the small bowel of an adult—a radiological sign of a serious post-operative complication.
    E. E. J. Smith, J. H. Saunders and N. Bowley
  The ultrasound diagnosis of hydatidiform mole and coexistent fetus associated with elevated maternal serum alpha feto protein.
    G. H. R. Lamb and R. Oakley

Correspondence. 269
  Use of diagnostic ultrasound to measure the lumbar spinal canal.
    J. A. Veiga-Pires, R. v. d. Beek and M. C. Kaiser; H. R. Stockdale and D. Finlay
  Gold grain dosimetry.
    C. Binks

Forthcoming events. 271

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
32 Welbeck Street, London W1M 7PG

ISSN 0007-1285
16283

14.9.82

Volume 54 Number 64
April 198

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis
Radiation oncology
Nuclear medicine
Ultrasound
Radiological physics
Radiobiology
Radiation protection
and related disciplines

LIBRARY

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01-836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01-935 6237 and 01-935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries

M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

For the attention of Ultrasound Users and Manufacturers

World Meeting on Ultrasound

Third Meeting of the World Federation
for Ultrasound in Medicine and Biology
at the spacious Metropole Conference Centre

Brighton, England
26–30 July, 1982

Exhibition space now available

for manufacturers of
ULTRASOUND EQUIPMENT
AND OTHER MEDICAL IMAGING MODALITIES

A World Conference combined with a Trade Exhibition

Reservations for space now being taken
Details from: Conference Consultants (London) Limited
4 "L" Portman Mansions
Chiltern Street, London W1M 1LF
Tel: 01-486 6582 Cables: DUOCON London W1

F. Schajowicz

Tumors and Tumorlike Lesions of Bone and Joints

1981. 948 figures, 2 color inserts. Approx. 650 pages
Cloth DM 318,–; approx. US $ 167.00
ISBN 3-540-90492-1
Distribution rights for Japan: Nankodo Co., Ltd., Tokyo

Contents: Introduction. – Bone-Forming Tumors. – Cartilage-Forming Tumors. – Giant-Cell Tumor (Osteoclastoma). – Marrow Tumors. – Vascular Tumors. – Other Connective Tissue Tumors. – Other Tumors. – Tumors Arising at Site of Pre-existing Bone Lesions. – Tumorlike Lesions. – Tumors and Tumorlike Lesions of the Synovial Membrane.

Destined to become a classic in its field, **Tumors and Tumorlike Lesions of Bone and Joints** is an up-to-date compendium of the clinical and radiologic features of these difficult disease entities. It summarizes the author's experiences in 40 years work in osteo-articular pathology. Under his guidance, over 6000 bone tumors and tumorlike lesions were studied and clearly documented at the International Reference Center of Bone Tumors of the World Health Organization, which used the WHO classification and definitions co-authored by Dr. Schajowicz. The detailed descriptions of histology featured in the book emphasize pathologic and clinical radiologic correlations and are accompanied by numerous photomicrographs, many in full color. Also included is information on the author's original technique for puncture (aspiration) biopsy, as well as reports on new tumor types (malignant osteoblastoma and mesenchymoma of bone) and new concepts on such tumor types as juxtacortical osteosarcoma, osteoid osteoma and osteoblastoma, giant cell tumor of bone, and Ewing's sarcoma. **Tumors and Tumorlike Lesions of Bone and Joints** will prove the ideal reference for pathologists, orthopedic surgeons, and radiologists who must frequently diagnose and treat tumors of the locomotor system.

1742/5/1

Springer-Verlag Berlin Heidelberg New York

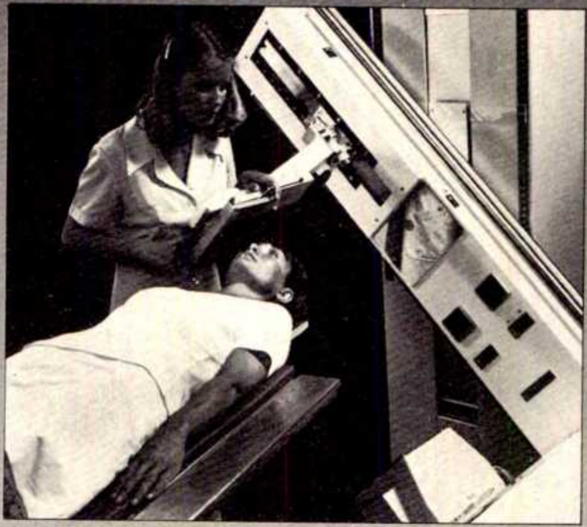
IT'S YOUR RESULT THAT MATTER.

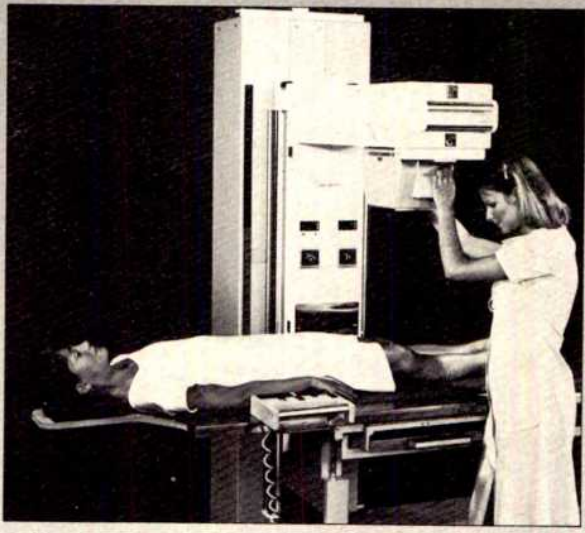
Speed and precision in skull and skeletal radiography.

The Pendo DIAGNOST is a robust economy class system for skull radiography in sitting and recumbent patients.

The freedom of movement in height and regulation of the pendulum arm allows fast and precise positioning for all skull projections.

Together with the special mobile coordinate table, TRAUMOB C, with floating table top, an ideal combination is achieved for skull radiography and bucky radiography with full body coverage. When changing over from special skull radiography to bucky work, the equipment is repositioned instead of the patient. This makes the system unique for traumatology.





Touch controls integrated in operation bars; bright digital read out for all coordinates and angulation; floating zero technique for the coordinates; isocentric working procedure; full instructions for standard and specialized projections further increase the ergonomy and the convenience in using the Pendo DIAGNOST system.

To get full details please mail the coupon.*

Philips Medical System cover the range of advanced diagnostic imaging and radiation therapy.

PHILIPS

PHILIPS **Medical Systems**

* UK enquiries: Philips Medical Systems, Kelvin House
63/75 Glenthorne Road, Hammersmith, London W6 OLJ.

I want INFORMATION about
the Pendo DIAGNOST and TRAUMOB C

ne

pital

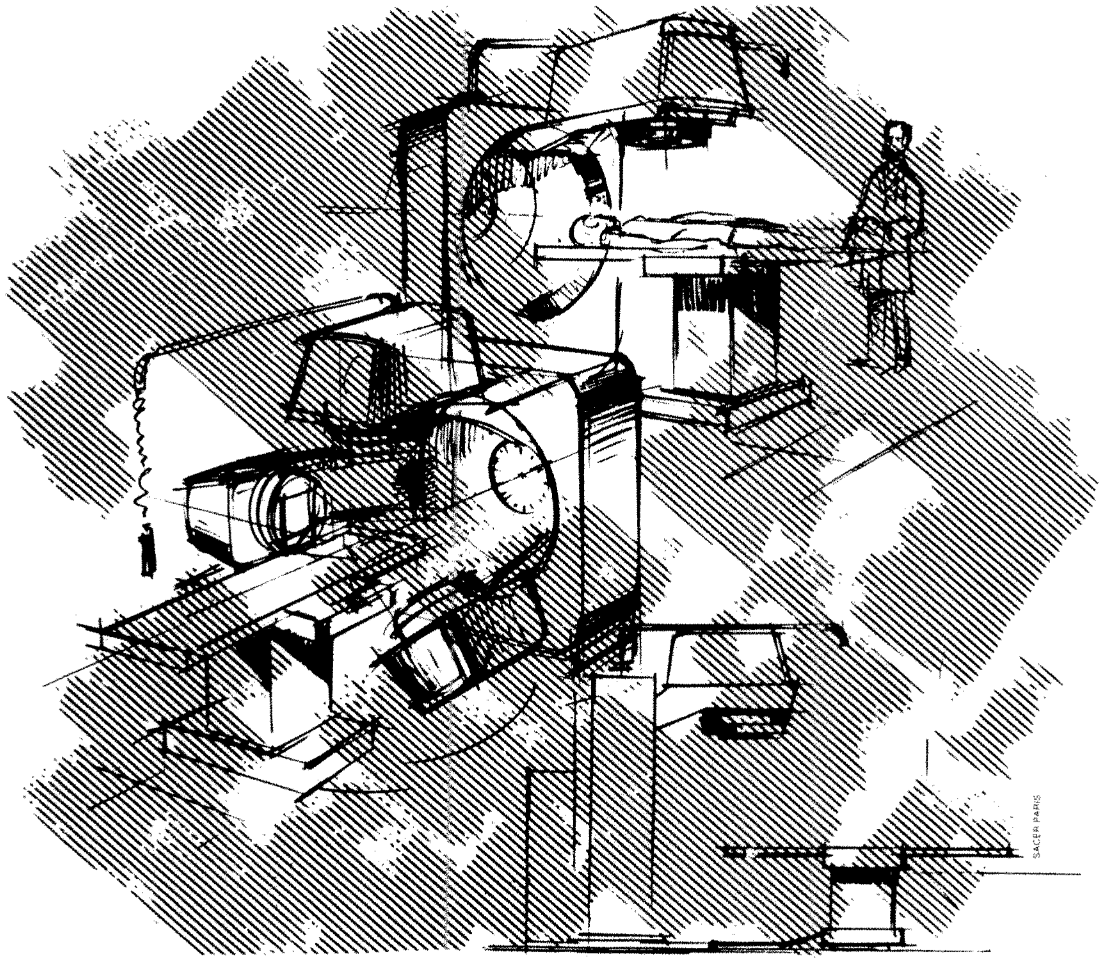
et

n

ntry

Philips Industries
dical Systems Division-QM
keting Communication
nt., Eindhoven, th
herlands BJ

A new design
...a new technology
yet easy to use and reliable



TELECOBALT
ALCYON
from
CGR

The Alcyon unit features easy installation (no floor pit required), easy servicing and easy exchange of sourcehead. It has 8,000 Rhm capacity, isocentric couch and is very competitively priced. The Alcyon fully complies with R.A.S.M.P. 75.

Full details of this and other treatment linacs from:
CGR MEDICAL LIMITED
Astronaut House, Feltham, Middx. Tel: 01-890 8166
Branches at Bristol, Cambridge, Edinburgh, Glasgow,
Manchester, Nottingham.

SIEMENS

When programmed x-ray diagnosis is preferred, we have the ideal combination

The multipurpose Siregraph C automatic x-ray table has enhanced routine diagnostic capability, including aniography of the body trunk and lower extremities.

The escutcheon of the Tridoros 712 MP generator puts all the radiographic parameters at your fingertips by means of microprocessor technology.

Programmed radiographic factors may be inserted by the Superintendent Radiographer or Radiologist and these factors are retained permanently under lock and key. This 70kW 12 pulse machine maintains high voltage accuracy yet offers extreme flexibility with provision for 49 programmes each for radiography and planigraphy.

For full details contact: Siemens Medical Group,
Siemens Limited, Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS. Telephone: (09327) 85691.

Siemens–the ultimate in cost effective x-ray diagnosis

Carcinogenesis and Radiation Risks: a Biomathematical Reconnaissance

by W. V. Mayneord, C.B.E., D.Sc., F.R.S. and R. H. Clarke, Ph.D.

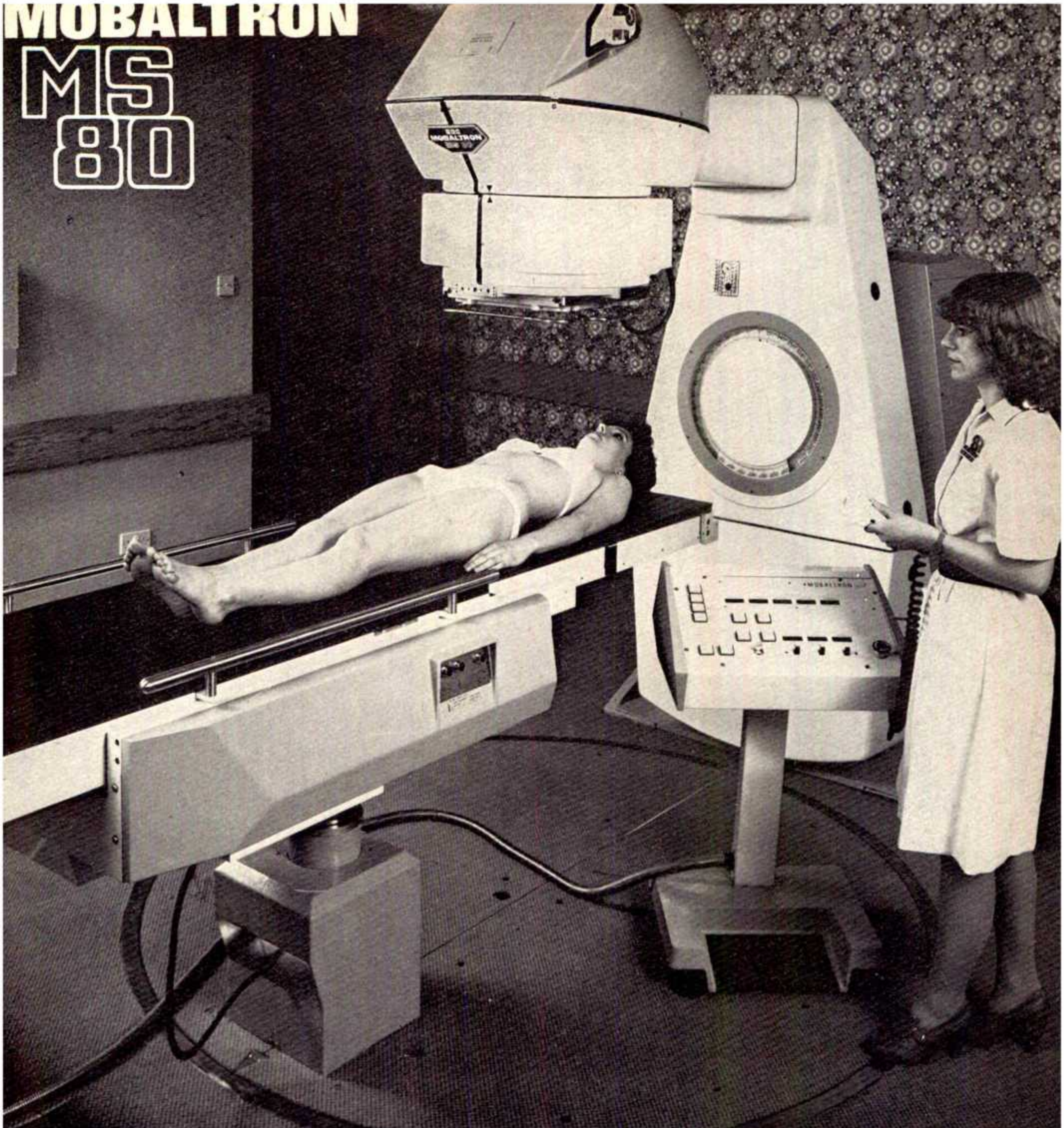
with foreword by Sir Eric Pochin, M.D.

British Journal of Radiology Supplement No. 12, 1975; reprinted 1979.

The first printing of this refreshingly original monograph by Professor Mayneord and Dr. Clarke was sold out. In view of the increasing interest in the topics dealt with by the authors, the work was reprinted. It explores some of the fundamental problems that arise when one attempts to predict the biological effects of a given dose of radiation. The authors point out that, in attempting an estimate of biological effect, for example carcinogenesis, it is frequently assumed that the risk is simply proportional to the dose received, although biological experiment often reveals a much more complex relation between effect and dose. They examine some of the consequences of taking such complex relationships into account in assessing "risk" on the basis of "dose" and propose a formula relating the risk to a whole population of cells from a rare event, such as the "transformation" of a single cell or group of cells. The parameters of the basic formula can be varied to meet particular assumptions regarding the distribution of dose in tissue and of response to dose. Using this formula, analyses are made of many different types of problem, including those presented by "point sources". It is emphasized throughout that the derivation of probabilities is not merely an exercise in mathematical physics but also involves cytology, genetics, immunology and hormone physiology, as well as studies of viral and chemical carcinogenesis. However, the method of analysis used leads to a clearer definition of the problems that have to be studied in attempting to produce more logical estimates of the risks from radiation, and the quantities of significance in designing experimental investigations.

The monograph represents a detailed development of ideas presented by Professor Mayneord in his Mackenzie Davidson Memorial Lecture of 1968 on "Radiation Carcinogenesis" and workers in the fields of radiobiology, experimental carcinogenesis and health physics will gain valuable insights from this study.

Orders to : Price **£6·50**
Publications Department, The British Institute of Radiology,
32 Welbeck Street, London, W1M 7PG (01–935–6237) or your bookseller.



MOBALTRON MS 80

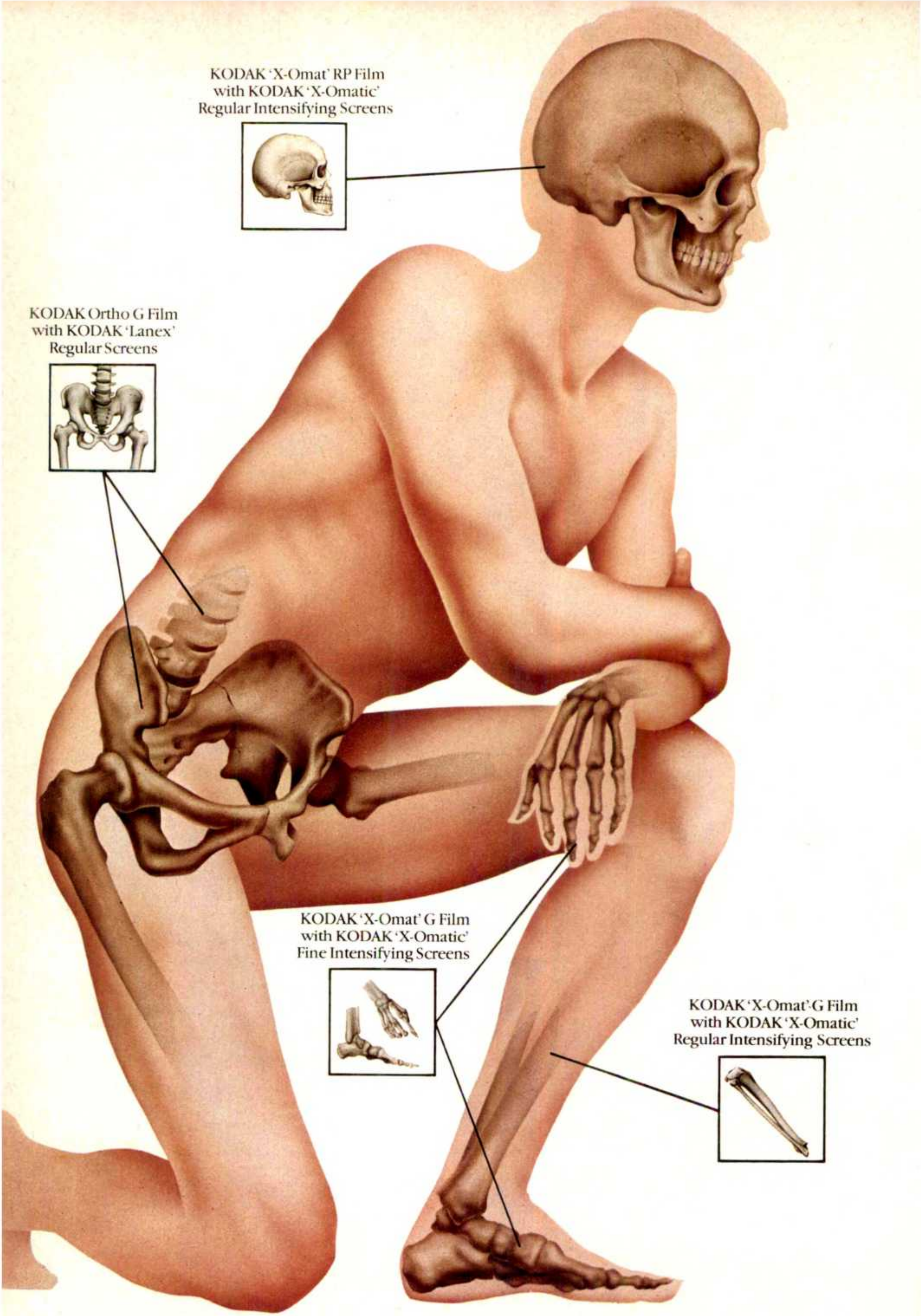
The Mobaltron M S 80 is one of the most sophisticated cobalt 60 units in the world, complying fully with R.A.S.M.P. 75 and having the following features:

- 40 x 40 cm field size at 80 cm.
- 10,000 RHM head capacity.
- Full interlock and confirmation circuits.
- Digital readouts.
- Dual timer.
- Variable speed motorised movements.
- Split spine treatment table.

The Mobaltron M S 80 can also be supplied as a computer controlled tracking unit.

TEM

TEM Instruments Limited
Gatwick Road, Crawley, Sussex. RH10 2RG, England
Tel: 0293 31244 Telex: 87397 Grams: TESTMENT CRAWLEY


KODAK 'X-Omat' RP Film
with KODAK 'X-Omatic'
Regular Intensifying Screens
KODAK Ortho G Film
with KODAK 'Lanex'
Regular Screens
KODAK 'X-Omat' G Film
with KODAK 'X-Omatic'
Fine Intensifying Screens
KODAK 'X-Omat' G Film
with KODAK 'X-Omatic'
Regular Intensifying Screens

Kodak bone radiography products from head to toe.

Kodak has the most comprehensive service network in the country.

We back that service with a range of products that includes over thirty diagnostic imaging films; and covers processors, cassettes, intensifying screens, chemicals and daylight handling equipment.

Kodak Service is there to help you maintain consistent image quality whilst containing costs.

In the working environment, this means we can aid with planning an efficient process area.

In human terms, we can help with the training of radiologists, radiographers and technicians: on your premises or at our own Marketing Education Centre.

Equipment maintenance is also an important quality control factor, and Kodak provides a highly competitive service from strategically located Sales Centres.

For details, speak to your Kodak representative.

He can give you up-to-date information on all areas of diagnostic imaging.

Kodak. We care about your image.

Kodak

KODAK 'Lanex' Regular Screens for special procedures are available to fit Puck, AOT and CGR rapid film changers. Kodak and all product names printed thus–'X-Omat'–are trade marks.

Diagnostic Radiologist

South Africa

Remuneration up to R60 000 p.a. plus numerous fringe benefits including company car

Applications are invited from Qualified Diagnostic Radiologists for this position with the Klerksdorp Mines Benefit Society, which provides medical care for approximately 11,000 gold mine employees and their families in this region.

Applicants should have experience in selective arteriography, ultrasun investigations etc. and should be doctors, qualified in Britain who have passed their British qualifications in Radiology. The Society utilises some of the most modern equipment available, and maintains the high standards associated with South African medical practice.

Remuneration and benefits offered

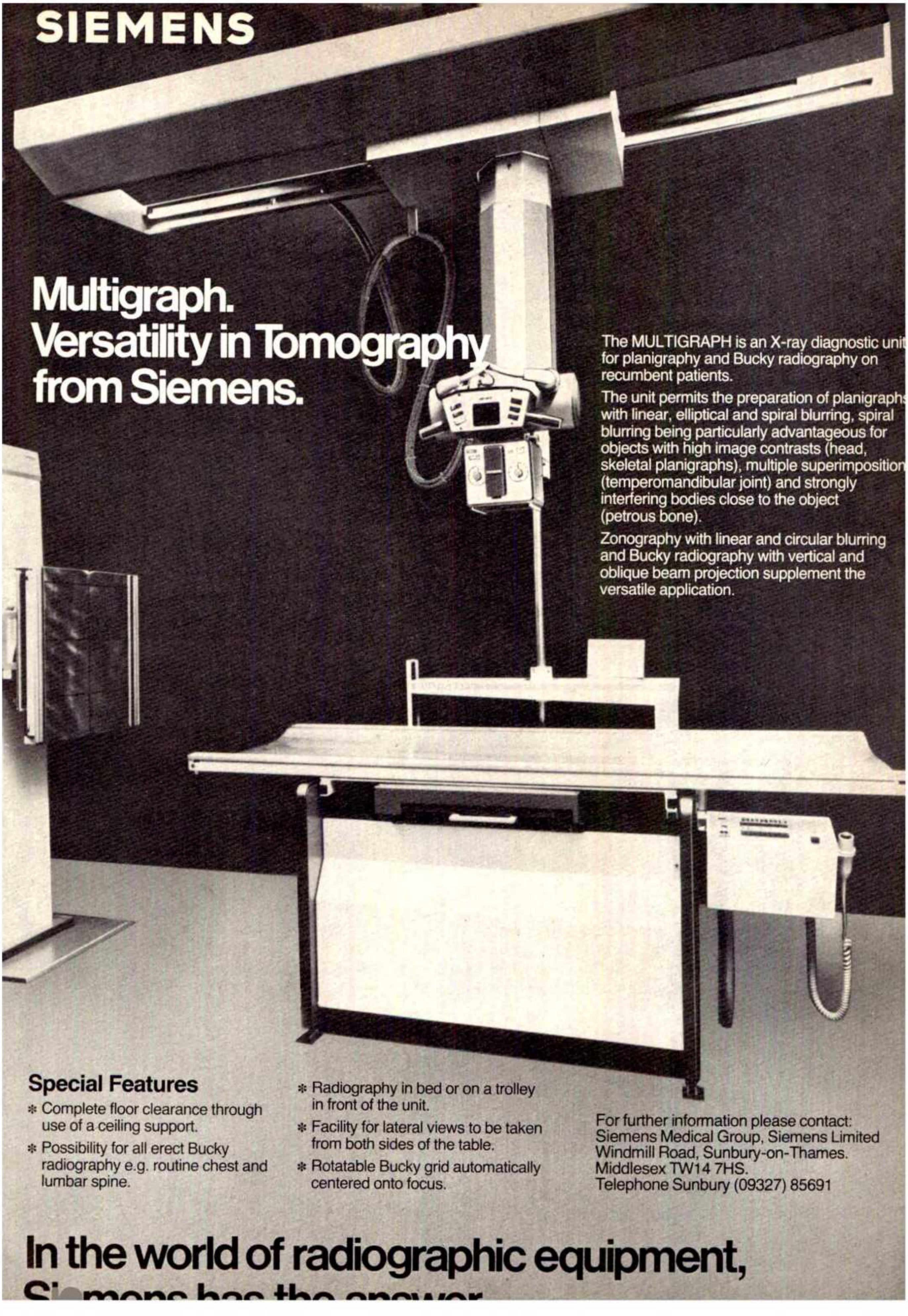
- Basic salary; according to experience.
- Membership of the Staff Provident Fund; towards which the employee contributes 7½% of basic salary and the Society 13%.
- Group insurance scheme; with a life cover of six times the basic, annual salary; premiums borne by the Society.
- Free accident insurance.
- Subsidised membership of medical benefit scheme.
- Annual leave of 35 working days - 5-day week. No night work.
- Car provided; to a maximum value of R10 000.
  Allowance for running expense of car R1 040 per annum.
- Assistance with accommodation and relocation expenses.

Klerksdorp is a medium-sized Transvaal town with all the facilities and amenities one would expect in a community of this size. Both private and government schooling is available, and the major international centre of Johannesburg is just over two hours drive away.

Applicants should send a brief C.V. with age, marital status, present position and experience to Mr S.A.A. Bryant,
Anglo Charter International Services
(Appointments Division),
40 Holborn Viaduct, London EC1P 1AJ,
quoting reference SBJ/23/81.

A personal interview will be arranged with prospective candidates in London. Full particulars of conditions of service will be made available to bona fide applicants.

KDM



SIEMENS

Multigraph. Versatility in Tomography from Siemens.

The MULTIGRAPH is an X-ray diagnostic unit for planigraphy and Bucky radiography on recumbent patients.

The unit permits the preparation of planigraphs with linear, elliptical and spiral blurring, spiral blurring being particularly advantageous for objects with high image contrasts (head, skeletal planigraphs), multiple superimposition (temperomandibular joint) and strongly interfering bodies close to the object (petrous bone).

Zonography with linear and circular blurring and Bucky radiography with vertical and oblique beam projection supplement the versatile application.

Special Features

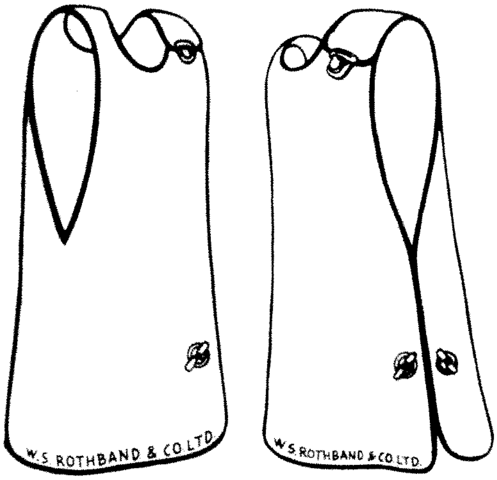
- Complete floor clearance through use of a ceiling support.
- Possibility for all erect Bucky radiography e.g. routine chest and lumbar spine.
- Radiography in bed or on a trolley in front of the unit.
- Facility for lateral views to be taken from both sides of the table.
- Rotatable Bucky grid automatically centered onto focus.

For further information please contact:
Siemens Medical Group, Siemens Limited
Windmill Road, Sunbury-on-Thames.
Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691

In the world of radiographic equipment, Siemens has the answer.

DOCTOR "C" TYPE DOUBLE-SIDED APRON

Right side closed, left side has push-in-clip shoulder fastening,
(or if "Velcro" preferred, please state on order).


W.S. ROTHBAND & CO. LTD.
W.S. ROTHBAND & CO LTD.

Super-flexible–Multi-layered.

Foam padded shoulders.

Standard size is 24 in (61 cm) wide. Ladies slim fitting 21 in (53 cm) also available.

Lengths, choice of 33 in (84 cm), 36 in (91 cm), 39 in (99 cm), 42 in (107 cm).

Washable PVC colours, choice of royal blue, white, green, yellow, red.

Lead equivalents, choice of 0.25 mm, 0.35 mm, 0.50 mm.

This Apron has been specially designed by our Company for operators who stand "right-side-on" and who require protection without a gap on the right hand side.

W. S. ROTHBAND & CO. LTD
Telephone 061–834 1303

21 Elizabeth Street
Manchester M8 8WT, England

Established 1860

A major new review

Bladder Cancer –
Principles of Combination Therapy
Edited by R T D Oliver, H J G Bloom and W F Hendry

Bladder Cancer concentrates particularly on new chemotherapeutic techniques of management. It contains much unpublished data originally presented at a recent international workshop organised by the Institute of Urology. Jointly edited by a urological surgeon, a radiotherapeutic oncologist and a medical oncologist, it will be essential reading for all those concerned with the management of this difficult condition.

1981 346 pages £25.00

Order now from your bookseller or by writing direct to

Butterworths Borough Green, Sevenoaks, Kent TN15 8PH

SHIMADZU URINOGRAPH

RELIABLE, ACCURATE UROLOGICAL X-RAY TABLE WITH FUNCTIONS AND FEATURES THAT ALSO COVER GENERAL RADIOGRAPHIC APPLICATIONS

The **URINOGRAPH** is an examination table that not only permits transurethral surgery, endoscope examination, and other routine tasks performed in urology and gynecology without resorting to X-ray examination, but also allows X-ray examination in combination with such medical treatment programs.
Besides ordinary radiography, the **URINOGRAPH** also permits TV fluoroscopy, spotfilming, oblique beam technique and tomography. Dose saving in fluorography through the use of an image amplifier is of particular importance in urology.

See SHIMADZU at the ICR-81, Brussels, June, 1981
Booth No. 9203 & 9302

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Düsseldorf 1, Johannes Weyer Str.1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

Clinical and Experimental Applications of Krypton 81m

Edited by J. P. Lavender

The British Journal of Radiology
Special Report 15

This work is composed of papers presented at an International Meeting held in June 1977 concerned with a new physiological tool; the use of a very short-lived radioactive gas krypton 81m.

Krypton 81m is a noble gas with a 13 second half life available from a portable generator with a half life of 4½ hours. Although known for a number of years it has only been used with any frequency by physiologists and clinicians since 1975.

The first section of the book deals with the production of the parent isotope rubidium 81 and the design of generators. The second section comprises a series of papers concerned with the use of the equilibrium image as both a picture and a measure of regional lung ventilation and perfusion. It also outlines problems of deriving absolute values of lung function. In the third section, papers illustrate the use of krypton 81m as a clinical tool in the diagnosis of pulmonary embolic disease and other pulmonary diseases and compare such information with that obtained from the more familiar xenon 133. In the last section the use of intra-arterial krypton as a marker of regional myocardial and cerebral blood flow is discussed. This technique, which has been most highly developed in the case of the myocardium, allows detailed images of the myocardial perfusion to be recorded. Perhaps its clearest application is in following rapid changes of regional myocardial perfusion in response to transient ischaemia, stress and drugs.

The discussion following each paper allows an assessment of the value and place of this new technique.

ISBN 0 905749 01 4
ISSN 0306–2120

Price £12

Orders to:

Publications
The British Institute of Radiology
32 Welbeck Street, London W1M 7PG
(01–935 6237)

or your local bookseller.

British Journal of Radiology

All enquiries for space should be addressed to:
Advertisement Department
The British Journal of Radiology
24a Litchfield Street
London WC2H 9NX
Tel. 01–836 5281
Telex 265972

University of Bristol

CHAIR IN RADIODIAGNOSIS

The University proposes to make an appointment to the Chair in Radiodiagnosis which will become vacant on 1st August, 1981, on the retirement of Professor J. H. Middlemiss.

Suitably qualified candidates are invited to submit applications by 1st May, 1981. Further particulars of the appointment may be obtained from the Registrar and Secretary,
University Senate House, Bristol BS8 1TH.

The French ANRT (Association Nationale de la recherche Technique)

May 19–20, 1981, PARIS
U.I.C., 14 Rue Jean Rey

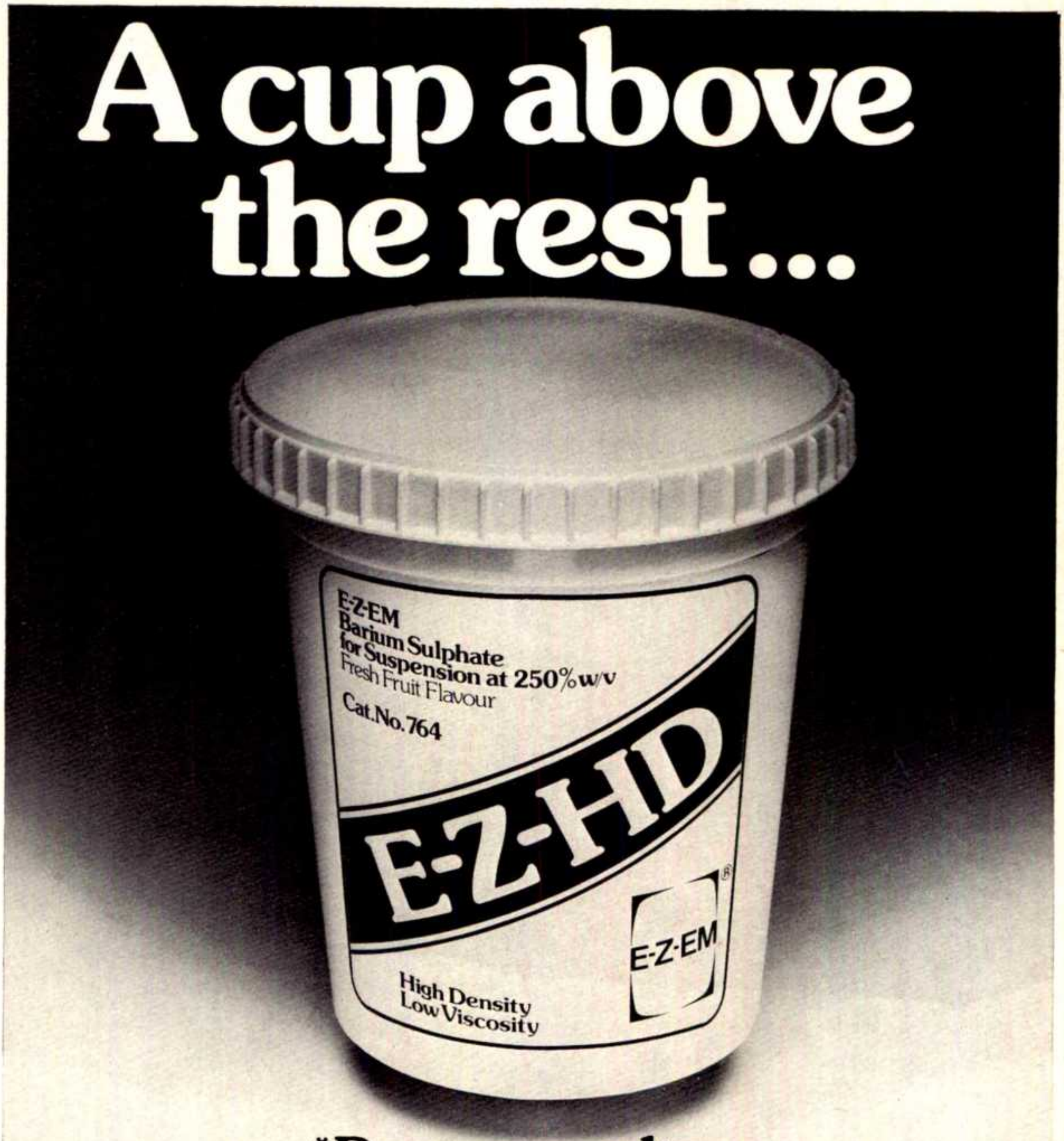
"1st European Conference on Cineradiography with Photons or Particles"

This conference will bring together all people involved in any new way in Radiography by Photons (X, γ) or Particles (neutrons...)
The main techniques concerned are those of Cineradiography, Flash Radiography, Scanning Radiography together with those of Tomography and 3D Reconstruction applied to any field like: Biomechanics and biology, Industry and Technology, Physics
The congress will include about 40 papers presented by French and foreign Specialists in each of the above-mentioned fields.

Additional Papers can be still proposed.

For further information, program, or proposal of paper, please contact:

Madame DIONISI
A.N.R.T.
101 Avenue Raymond Poincaré
75116 PARIS
Telephone: (1) 5017227



***Proven results.**
Just add water and shake.

E-Z-EM ®

*Assessment of the Double Contrast Barium Meal: Method and Application. *Lintott et al. Clin. Radiol. (1978) 29, 313—321*

*A new method for studying barium sulphate contrast media *in vitro.* Some factors contributing to the visualization of areae gastricae By Pekka Virkkunen and Minna Retulainen *1980, British Journal of Radiology, 53, 765—769.*

Full details from:

Henleys Medical Supplies Ltd. London N8 0DL Tel: 01-889 3151

PL/1665/0003

Produced by E-Z-EM Ltd London

IT'S RATHER FUN BEING
A SMALL FIRM . . .

. . . so that a letter written to the "Times" of London (Business News, September 16th 1980) extolling your virtues gives every member of the staff a personal glow of pleasure.

. . . so that an envelope from Kenya addressed only
CUTHBERT ANDREWS, U.K.
which reaches you within fifteen days can cause a giggle that you can be *that* well known.

. . . so that a formal request to provide a reference for the credit-worthiness of one of the largest and best-known U.K. giants can never be quite forgotten.

. . . so that *your* order can be seen and discussed by everyone before being entered and executed.

. . . so that you can produce a catalogue with, so we are told, personal touches not generally thought quite dignified by large concerns. By the way, have you had your copy of the Eleventh (Golden) Edition of EVERYTHING X-RAY?

. . . so that the recent retirement of our oldest employee Harry Bentley, after a friendship of thirty-five years, is felt by all – and by many suppliers and customers in the London area also, for whom he always had the latest story.

Small we may be
but we're not called Everything X-ray for nothing!

CUTHBERT ANDREWS
EVERYTHING X-RAY LTD.

5 HIGH STREET, BUSHEY VILLAGE, WATFORD WD2 1BE

Overseas telegrams:
EXRAYZE WATFORD

Telephone:
01–950 2525

Telex:
925859 Elwood G

1981, *British Journal of Radiology*, *54*, 277–288

VOLUME 54 NUMBER 640 APRIL 1981

The British Journal of Radiology

The radiographic detection of acute pulmonary oedema. A comparison of radiographic appearances, densitometry and lung water in dogs

By P. D. Snashall, B.Sc., M.D., M.R.C.P., Suzanne J. Keyes, Barbara M. Morgan, *R. J. McAnulty, †P. F. Mitchell-Heggs, M.A., Ph.D., M.R.C.P., J. M. McIvor, M.B., B.Ch., F.R.C.R. and K. A. Howlett, M.B., B.Ch., F.R.C.R.

Departments of Medicine and Radiology, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, *Cardiothoracic Institute, Brompton Hospital, Fulham Road, London SW3 and †Department of Medicine, Epsom District Hospital, Dorking Road, Epsom, Surrey

(*Received June 1980 and accepted November 1980*)

ABSTRACT

We have induced acute pulmonary oedema in upright anaesthetized dogs by increasing pulmonary microvascular permeability or by extacellular fluid volume overload in order to determine the sensitivity and specificity of the radiograph to the presence of abnormal lung water. Radiographs were taken before and after development of oedema. At the end of the experiment we removed the inflated lungs and froze them in liquid nitrogen and subsequently examined them macroscopically in the frozen state. The extravascular water/dry lung weight ratio was measured gravimetrically on seven portions of each lung. Final radiographs were examined by two radiologists with and without the base-line films for comparison. We directly measured the change in opacity of the films with a radiographic densitometer. When a dog's mean extravascular water/g dry lung was increased by more than 35% it was invariably recognized, in one or more zones, as definite oedema. Control dogs were reliably recognized as normal when base-line films were used but the distinction between normal and minor degrees of oedema could not be made without the base-line films. There was a positive correlation between radiological grade and lung water, but a great deal of overlap between grades. Densitometry was not a sensitive or reliable method for diagnosing or quantifying oedema. Oedema was usually associated with a decrease in volume of the lower lung zones.

The sensitivity of the chest radiograph in the detection of pulmonary oedema has never been adequately determined. It is commonly assumed that the radiograph is insensitive and that significant pulmonary oedema, causing tachypnoea, lung crackles or hypoxia may exist in the absence of radiographic abnormalities. Fishman (1976) has suggested that lung extravascular water must be increased by 300–600% before oedema becomes detectable. Harrison *et al.* (1971), however, stressed the sensitivity of the radiograph in the detection of acute pulmonary oedema after myocardial infarction. They showed that the radiographic appearances of pulmonary oedema may frequently precede clinical signs, whereas the radiograph was always abnormal when clinical signs were present. This conclusion was supported by Pistolesi and Guintini (1978) who compared radiographic grading of cardiogenic pulmonary oedema with extravascular lung water measured by a modified double-indicator dilution technique. The radiograph was frequently abnormal in patients with minimal oedema or where lung water was within the normal range; when lung water was increased by more than 50% there was an approximately linear relationship between water and radiographic grade. Their conclusion is dependent on the supposition that their method for measuring extravascular lung water in diseased lung is valid.

Our aim has been to determine the sensitivity and specificity of the radiograph in the detection of abnormal lung water, measured gravimetrically in an animal model. We have used upright, anaesthetized dogs in which we have induced pulmonary oedema either by extracellular fluid volume expansion or by increasing microvascular permeability. In addition to having the films assessed independently by two radiologists, we have used densitometry of the films to obtain an objective quantitation of the radiographic changes.

METHODS

We have studied 23 mongrel dogs of either sex weighing 18–25 kg (mean weight=22.1 kg). After inducing anaesthesia with intravenous thiopentone sodium (20 mg/kg), dogs were intubated with a cuffed endotracheal tube and anaesthesia was maintained with halothane (0.5%) while gluco-chloralose (Merck, Darmstadt) (40 mg/kg) was slowly injected intravenously. Subsequent light anaesthesia was maintained with chloralose (10 mg/kg) every two to three hours as required. The dogs breathed air spontaneously throughout the experiment. We then catheterized the femoral artery and vein. A double lumen balloon catheter was inserted under fluoroscopic control into a pulmonary artery via the right external jugular vein. End tidal PCO_2 was monitored with an infrared medical gas analyser (Model LB-1, Beckman). Arterial blood was taken for measurement of pH, PO_2 and PCO_2 (Blood Gas Analyser Model 165, Corning Eel). Pulmonary and systemic arterial pressure and pulmonary wedge pressure were measured using strain gauges (Statham P23A 114) and recorded continuously on a multi-channel recorder. The pressures were measured from a zero reference pressure at the level of the left atrium as estimated from radiographs. In addition, in most dogs, a Cournand (French gauge 7) catheter was placed in the main pulmonary artery for injection of angiographic contrast medium. The animal was then placed in a vertical, head up position. We firmly bandaged the abdomen and hind limbs to prevent blood pooling.

We took AP and RL chest radiographs with a narrow (0.3 mm) focal spot tube (Siemens, Sunbury-on-Thames, Middlesex) with the chest inflated to 15 cm H_2O. The focus-film distance was 180 cm, so that the distance from focus to mid-point in the thorax was approximately 170 cm. Depending on the size of the dog, the settings of the X-ray tube were for the AP radiographs, kV 70–78 and mA 100, exposure time 0.064 second. The same settings were used before and after induction of oedema and an aluminium step wedge was included on each film for calibration of film density. To prevent the dog from breathing at the moment of exposure, we used artificial hyperventilation with an "Ambu" bag for a few seconds before the exposure. We timed the radiographs to coincide with end-diastole using a cardiac phase correlator (Nycotron, Oslo, Norway).

In most dogs AP and RL pulmonary angiograms were performed using 25 ml of sodium iothalamate (70% w/v) (Conray 420; May and Baker Limited, Dagenham, Essex), injected at 344 kPa (50 p.s.i.) at an inflation pressure of 15 cm H_2O.

Induction of oedema

We originally planned on three groups: control, oedema due to extracellular fluid volume (ECFV) expansion and oedema due to increased microvascular permeability produced by alloxan. However, several of the "control" animals developed slight patchy oedema and we believe that this was due to microvascular damage from pulmonary angiography. Therefore we did further true control experiments without angiography and we avoided the use of angiography in subsequent ECFV expansion experiments. Thus we have four experimental groups.

1. *Alloxan group* (n=7). Alloxan (Eastman Kodak, Rochester, NY) 75 mg/kg was injected intravenously in saline. We allowed 90–180 min for oedema to develop.
2. *Extracellular fluid volume expansion group* (n=6). We gave Hartmann's solution at a rate of 2 ml/kg body weight/minute. The volumes infused were 15–35% body weight in different dogs (15% $n=2$, 20% $n=1$, 30% $n=2$, 35% $n=1$). After completion of the infusion we waited between 20–40 minutes for the return of the pulmonary vascular pressures to base-line levels.
3. *Angiography group* (n=5). In these animals (the original control group) we performed pulmonary angiography alone. These dogs received an average of 70 ml of sodium iothalamate (70% w/v). We waited 90–120 minutes after the base-line angiograms for the oedema to develop.
4. *Control group* (n=5). These dogs received no oedemogenic agent but in all other respects the experimental procedure was identical in this group. They were suspended in the upright position for between 90–180 minutes.

At the end of the experiments we repeated the radiographs and blood gases and then immediately killed the dogs with intravenous pentobarbitone sodium. The lungs were exposed by a median sternotomy and inflation was maintained with an airway pressure of 15 cm H_2O (1.5 kPa). They were rapidly removed after hilar clamping and plunged into liquid nitrogen (−196°C). Simultaneously, a sample of heparinized blood was taken from the right heart.

EXAMINATION OF RADIOGRAPHS

Examination by radiologists

The films were examined independently by two practising and experienced general radiologists, one of whom had a particular interest in chest radiology. Their assessments were "blind" in the sense that although they were aware of the experimental design and the methods used to produce oedema, they were unaware of the procedures used on individual animals. They were aware from previous discussions that oedema was frequently associated with a decrease of lung volume.

They made two separate assessments. In the first, the final AP and RL films from each animal were examined without the base-line films for comparison. The films were examined for abnormal hazy shadowing, for which separate assessments were made in five areas of the films. These zones were: on the AP films, the parts of the right and left lungs, above the heart (zones I and II) and below the heart (zones III and IV); on the RL film below and posterior to a line drawn between the anterior costophrenic angle and the body of the fifth thoracic vertebra (zone V). We chose these zones after examining tantalum bronchograms that we performed on ten upright dogs as part of a separate study. The bronchograms, by outlining the lobar anatomy, have demonstrated that zones I and II contain only the upper lobes; zones III and IV the lower third of the lower lobes and zone V, both lower lobes. In these zones hazy shadowing was assessed as follows: Grade 0=normal; Grade 1= possible (apparently abnormal shadowing but insufficient to blur or obscure vessel shadows, cardiac or diaphragmatic outlines); Grade 2= definite (shadowing causing blurring and obscuring of vessel, cardiac and diaphragm outlines but involving less than half of the zone); Grade 3, as with Grade 2 but involving more than half of the zone; Grade 4, gross opacification with obliteration of all markings and boundaries. In a second assessment, each radiologist was presented with both baseline and final films. The assessment of hazy shadowing used the same zones and the same criteria for grading. They also looked for changes other than hazy shadowing, vessel blurring, airway cuffing and septal lines. Where possible they measured changes in width of vascular markings.

Examination with a densitometer

With a radiographic densitometer (type 2526, Nuclear Enterprises, Sighthill, Edinburgh) we measured density of films taken in base-line and final periods. We identified the same area of lung on each film by reference to vascular markings and avoided ribs. We made two or three measurements in each of the zones assessed by the radiologists. Each measurement included an area of film 6 mm in diameter. In addition, we measured the radiographic densities of the step wedge and used these readings to draw a calibration line, on semi-logarithmic paper, for each film. With this line we converted lung density values to equivalent aluminium thickness.

Volume changes measured from the radiographs

We noticed during the course of the experiments that diaphragmatic elevation frequently occurred as lungs became oedematous. We therefore attempted to measure from the radiographs the changes in lung volume occurring in the upper and lower lung zones. The measurement of these volume changes was made by comparing distances between an intrapulmonary marker (generally the bifurcation of a pulmonary blood vessel) and the pleural surface in three directions using the AP and RL angiograms or plain radiographs. The same intrapulmonary marker was used in the base-line and final films. The product of the three dimensions gives a "volume" which may be compared before and after oedema if one assumes that no change of shape in that region of lung has occurred. This technique has been validated as a means of measuring regional lung volumes (Snashall *et al.*, 1980).

Examination of frozen lungs

We examined the lungs in a cold room at −20°C. Each lung was divided into seven portions, these being upper and lower portions of the upper lobe, the middle lobe, and upper, middle and basal thirds of the lower lobe. The lower third was divided into anterior and posterior portions. Each portion was examined macroscopically for presence, size and distribution of perivascular and peribronchial cuffs of oedema.

ANALYTICAL METHODS

Water content and dry weight of blood-free lung

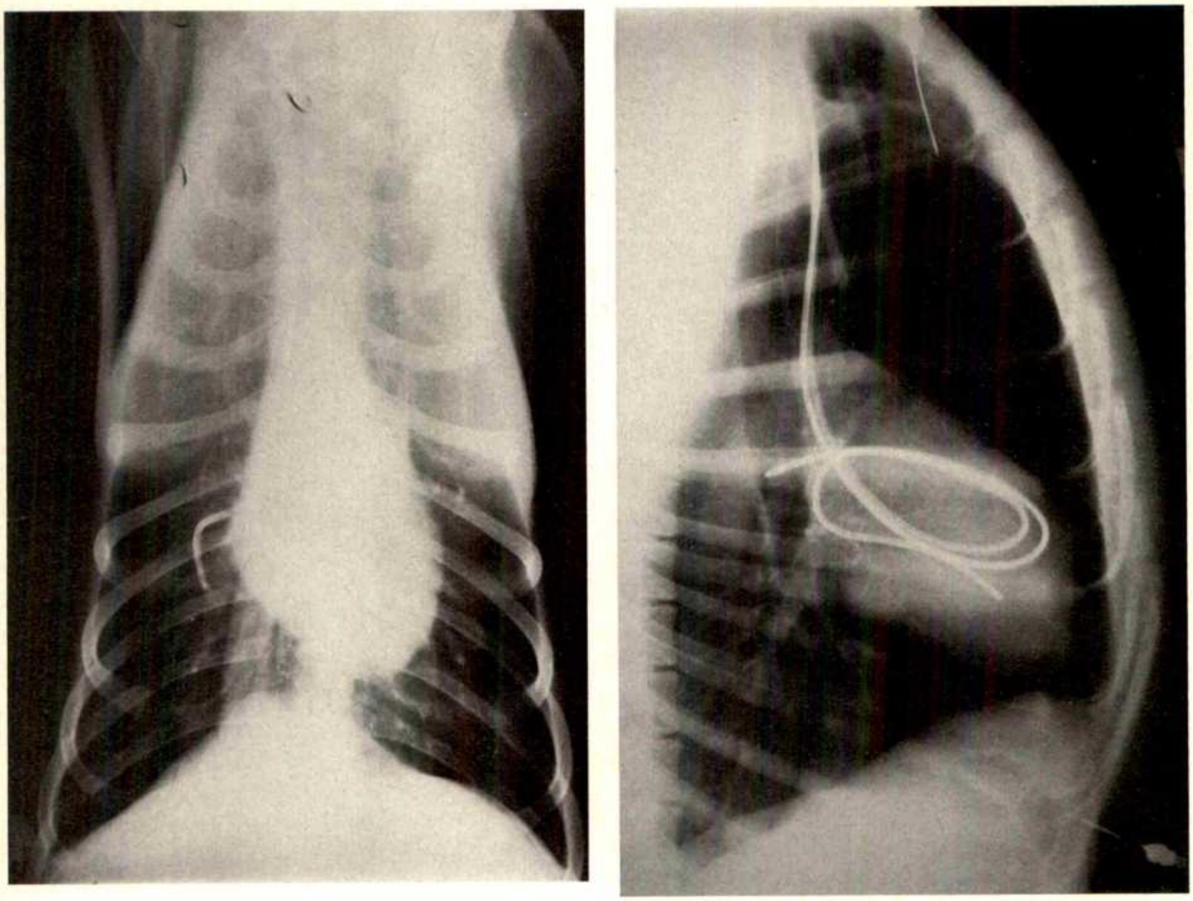
Each of the seven portions of lung was homogenized separately in a blender (Model L2R, Silversons Machines, Chesham, Buckinghamshire) and then samples of approximately equal amounts of each homogenate were poured into thick-walled polycarbonate tubes and centrifuged at 35 000 g (Model RC2-B, Dupont Sorvall, Hitchin, Herts) for one hour at 5°C. We measured the haemoglobin of the supernatant and the final blood sample by the standard cyanmethaemoglobin method (Model LCP, Fisons, Loughborough, Leicestershire). We determined the water content and dry weight of the seven samples of homogenate, supernatant and final (right ventricular) blood by drying in an oven at 90°C for 48 hours.

CALCULATIONS

Extravascular lung water

Essentially our method was that of Pearce *et al.* (1965) and our calculations, those of Selinger *et al.* (1975). The extravascular lung water and dry lung

UNIVERSITY COLLEGE OF MED
LIBRARY



A FIG. 1. B

weight were calculated for the seven portions separately. We have used the ratio of extravascular water/dry lung weight as our index of oedema.

Statistics

The significance of differences of paired data were tested by the paired t-test and a significance level $p < 0.05$ was accepted as indicating a significant difference. We calculated regression lines by the least squares method. We compared the number of zones assigned to each grade by the two radiologists, using the chi-square test. We tested the significance of differences between lung water values at different radiological grades with a single factor analysis of variance.

RESULTS

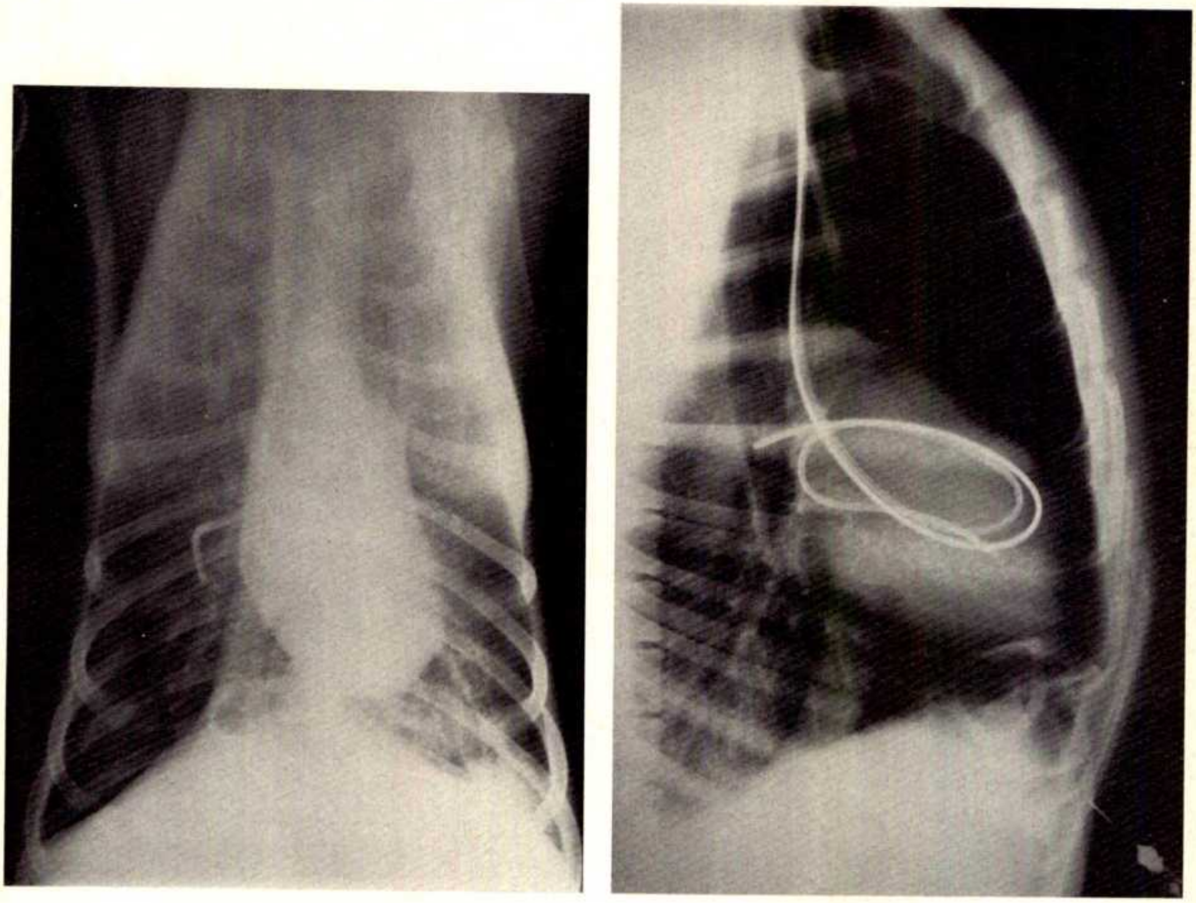
Lung water and the development of oedema

1. *Control group.* The mean extravascular water/dry lung weight ratio in control dogs was 4.3 ± 0.3. Within individual lungs there was little variation between the seven portions analysed (coefficient of variation = 0.07). Macroscopic examination of all lungs was normal but small perivascular cuffs of oedema were seen microscopically in two dogs. Despite the dogs being upright for 90–180 minutes, water contents of the upper and lower lobes were not significantly different (mean extravascular water/dry lung weight ratio of upper lobes = 4.1 ± 0.6) neither was there a significant difference between the top of the upper lobe (mean = 4.2 ± 0.2) and the lowest portion of the lower lobe (posterior basal portion, mean 4.3 ± 0.4).

2. *Alloxan group.* Immediately after the injection of Alloxan, pulmonary arterial pressure (Ppa) rose sharply (mean rise = 25 ± 4 cm H_2O and returned to base-line level in 21 ± 13 minutes). Wedge pressure (Pw) showed little change (mean rise = 5 ± 4 cm H_2O). At the time of the final radiographs Ppa and Pw were both approximately 3 cm H_2O above their base-line levels.

Macroscopic examination of the frozen lungs showed perivascular cuffs of oedema in all dogs and peribronchial cuffs in those with the most severe oedema. In two dogs with gross oedema, the lower lobes were solid and unaerated and could only be cut with a saw. Mean extravascular water/dry lung weight ratio was 8.9 ± 3.8). While in some dogs extravascular water was increased more at the bases than the apices, in other dogs no such gradient was seen.

3. *Angiography group.* Injection of contrast medium usually caused transient bradycardia, Ppa rose by 15 ± 11 cm H_2O and Pw by 5 ± 4 cm H_2O. At the time of the final radiographs Ppa was an average 5 cm H_2O above the base-line level. One dog developed severe oedema in the right



C D

FIG. 1.

AP and lateral radiographs of one dog before (A, B) (opposite) and after (C, D) (above) development of pulmonary oedema due to Alloxan. There is increased hazy shadowing at the left base recognized by both radiologists as definite (Grades 2 and 3) oedema. Extravascular water/dry lung weight in this zone = 8.2. The changes in the right basal zone were considered by both radiologists to indicate possible oedema (Grade 1); extravascular water/dry lung weight ratio = 5.3. Both upper zones were considered normal (Grade 0); extravascular water/dry lung weight ratio = 5.0 (right) and 4.5 (left). Note the upper zone shadowing due to overlying soft tissue. There is an apparent upward movement of the diaphragm with the development of oedema; loss of lower zone volume = 15%. The volume of the upper zone did not change. There was no change in width of vascular markings.

lung after two 25 ml injections of contrast medium into the right pulmonary artery. The left lung was normal. In three of the four less oedematous dogs macroscopic examination of frozen lungs was normal. Small perivascular cuffs were seen in the remaining dog. Mean extravascular water/dry lung weight ratio of the whole group was 4.8 ± 0.6 which was not significantly different from the control group.

4. *Volume loaded group*. Ppa and Pw rose rapidly for the first 15 minutes of the infusion and thereafter more slowly. At 50 minutes (when 10% body weight had been infused) Ppa had risen by 24 ± 6.3 cm H_2O and Pw by 21.5 ± 1 cm H_2O. When the infusion was complete Ppa and Pw returned to their approximate base-line levels in 31 ± 13 minutes. At the time of the final radiographs both Ppa and Pw were approximately 3 cm H_2O above base-line levels.

Microscopic examination showed perivascular cuffing in all lungs. In one dog these cuffs were blood-stained. Two dogs had peribronchial cuffs. Mean extravascular water/dry lung weight was 7.3 ± 4.6.

Examination of radiographs

Lung volume changes. Many dogs showed an obvious reduction in lung volume as oedema developed (Fig. 1). By observing the position of pulmonary vessels we have found that this loss of volume occurred exclusively in the lower zones of the lung, and was seen in all oedema groups, but not in control dogs (Fig. 2). There was a significant inverse relationship between lung water and lung volume, but there was considerable scatter (Fig. 3) ($r = -0.45$; $p < 0.05$). In general, fluid volume expansion and angiography produced more loss of lung volume for a given amount of oedema than alloxan. In one alloxan-treated dog and one fluid volume expanded dog massive oedema prevented the measurement of volume change.

Examination by radiologists

Agreement between the two radiologists. There were no statistically significant differences between the assessments made by the two radiologists on the lower zones of the lungs, with and without comparison with base-line films. Their upper zone assessments, however, differed significantly and these differences were particularly marked when the base-line film was not used for comparison.

TABLE I

GRADING OF CONTROL DOGS. NUMBERS OF GRADES IN EACH ZONE ASSESSED BY BOTH RADIOLOGISTS

		Grade				
		0	1	2	3	4
With base-line films	Upper zone	20	0	0	0	0
	Lower zone	29	1	0	0	0
Without baseline films	Upper zone	9	1	8	2	0
	Lower zone	20	10	0	0	0

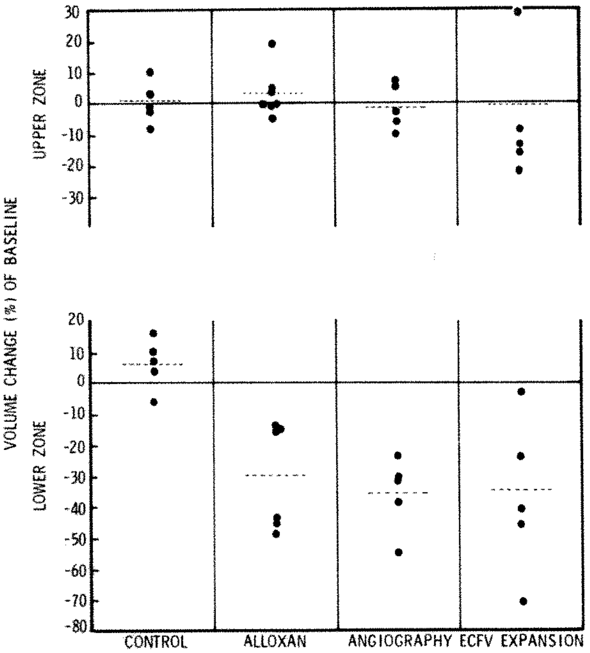


FIG. 2.

Relationship between changes in zonal lung volume in the four groups of dogs. In control dogs there is no loss of volume in upper or lower zones. Oedematous dogs show a large loss of lower zone lung volume, without significant upper zone changes. Mean volume change for each group is shown (——).

Assessment of control dogs. Virtually all zones of all the control dogs were graded 0 by both radiologists when using the base-line film for comparison (Table I). Without the base-line film control dogs were not reliably recognized as normal. Upper zones were particularly difficult in this respect.

Assessment of oedematous dogs. No differences of pattern of distribution of oedema were noted between oedema due to increased microvascular permeability, or that due to extracellular volume expansion. However, increases of hazy shadowing were more marked when there was a considerable change of lung volume. Thus, oedema due to volume loading or due to angiography where lung volume changes were relatively greater was more easily recognized.

Assessment of oedema using base-line films for comparison. The mean zonal extravascular water

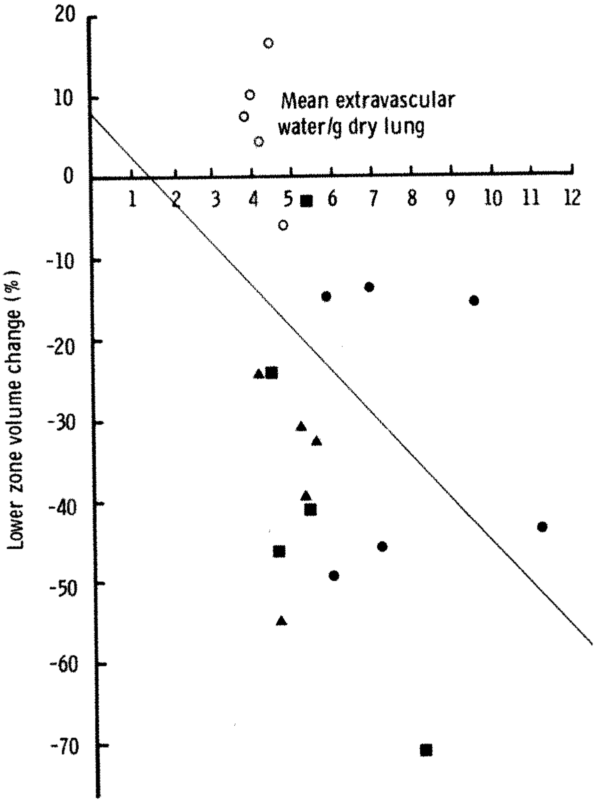


FIG. 3.

Relationship between extravascular water and lower zone volume change ($y = 5.4x + 8.2$; $r = -0.45$; $p < 0.05$) in individual dogs. Control dogs (○); oedema due to Alloxan (●); angiography (▲); extracellular fluid volume expansion (■).

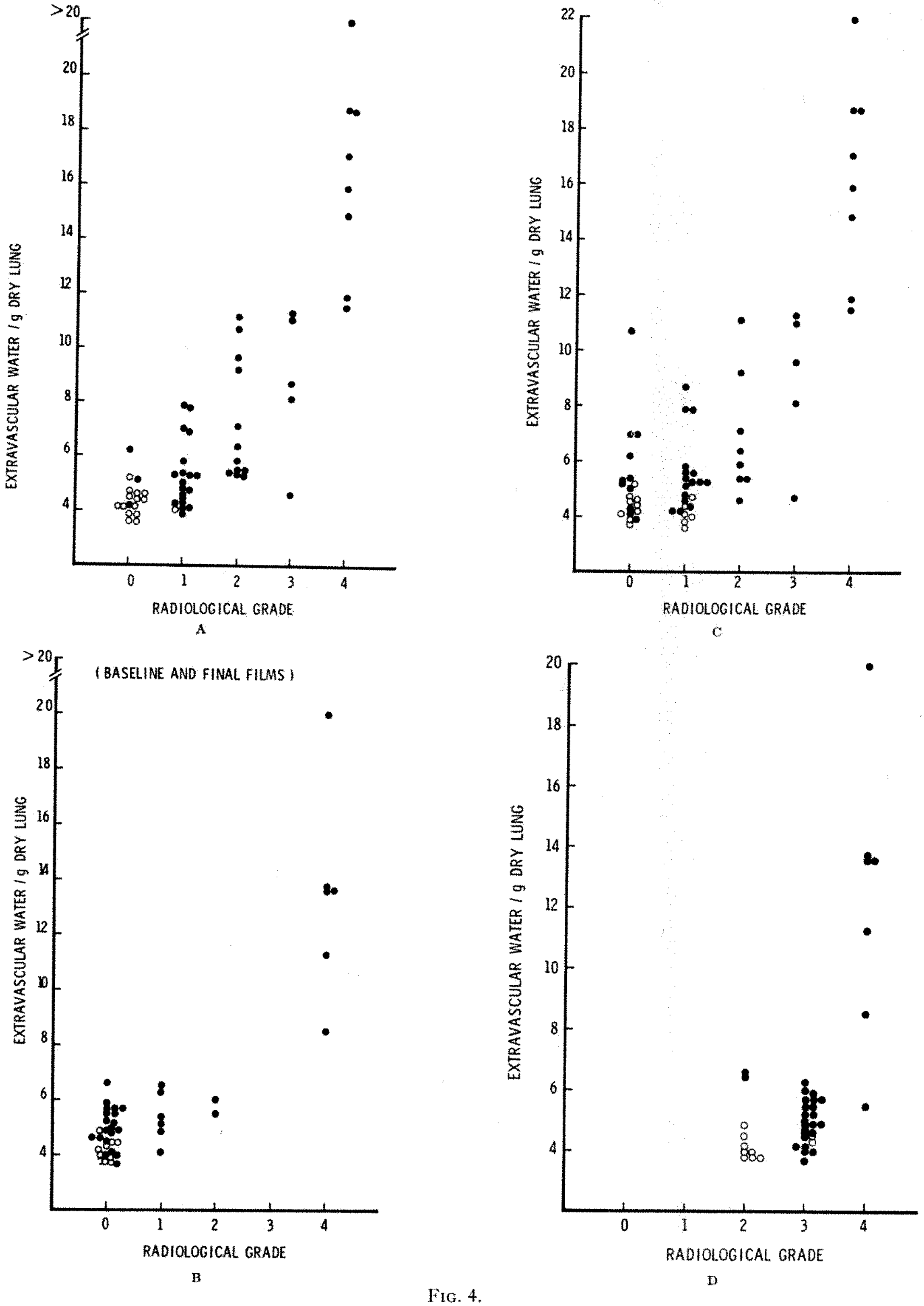


FIG. 4.

Relationship between one radiologist's grade and extravascular water/g dry lung. (A) lower zones with base-line films for comparison; (B) upper zones with base-line films for comparison; (C) lower zones without base-line films; and (D) upper zones without base-line films. Zones from control dogs = (○); from oedematous dogs = (●).

TABLE II

MEAN LUNG WATER AT EACH GRADE IN UPPER AND LOWER ZONES. THE VALUES SHOWN ARE MEAN % ZONAL EXTRAVASCULAR WATER/G DRY LUNG WITH RANGE IN ( ). THIS TABLE POOLS THE ASSESSMENTS BY THE TWO RADIOLOGISTS

		Grade				
		0	1	2	3	4
With base-line films	Upper zone	4.5 (3.7–6.6)	5.7 (4.0–6.6)	6.0 (5.5–20.0)	12.45 (8.5–13.8)	13.6 (8.5–20.0)
	Lower zone	4.3 (3.6–7.0)	5.3 (3.9–11.1)	6.3 (5.3–11.3)	11.0 (4.6–26.7)	16.5 (11.5–26.7)
Without base-line films	Upper zone	4.5 (3.7–6.6)	4.8 (3.8–6.5)	4.5 (3.8–6.6)	4.9 (3.7–13.6)	13.6 (5.5–20.0)
	Lower zone	4.65 (3.8–10.7)	4.7 (3.6–8.7)	5.9 (4.6–11.1)	11.0 (4.7–11.5)	16.5 (11.0–26.7)

values at each radiographic grade are shown in Table II. The relationship between one radiologist's grades and extravascular water in upper and lower zones are shown in Fig. 4. Although there was clearly a general relationship between grade and water, there was a considerable overlap of lung water between grades. The highest lung water content associated with a normal assessment (Grade 0) was 7.0; the lowest lung water content associated with definite oedema (Grade 2) was 5.3. The range of lung water associated with possible oedema (Grade 1) was particularly wide and in some zones a water content of up to 11.3 produced only a suspicion of oedema. There was little difference in the grading of oedema between upper and lower zones except that in the upper zones there were more Grade 0 assessments made on dogs with minimal oedema.

A closer relationship between lung water and oedema grade was seen when each dog's mean extravascular lung water/dry weight ratio was related to its highest zonal oedema grade (Fig. 5). The relationship is curvilinear and shows that the radiograph becomes abnormal before total extravascular lung water is more than minimally increased. When one or more zones in one dog were assessed as showing definite oedema (Grade 2), mean extravascular water/dry weight ratio was always greater than 4.5. When no zones showed definite oedema, lung water was always less than 5.8. No oedematous dogs were graded as normal (Grade 0). Four out of five control dogs were graded 0 by both radiologists. The remaining control dog was graded 0 by one radiologist and Grade 1 by the other on the basis of one dubious zone.

Assessments without base-line films. In the upper zones gross oedema could be reliably recognized but it was very difficult to recognize minimal oedema (Fig. 4D, Table II) and the two radiologists differed widely in their assessments. In the lower zones the assessment of definite and severe oedema (Grades 2, 3 and 4) was similar to that when base-line films were used, but it was not possible to distinguish between normal and minor degrees of oedema (Fig. 4C).

Changes in width of vascular markings. There were no changes in vessel width observed in the control or angiography groups. In the Alloxan-treated group, in three out of four dogs in which vessels could be clearly visualized there was an increase (mean 27%) in width of vascular markings. The fourth dog showed no change. However, in the extracellular volume expanded group in three out of four dogs in which vessels could be seen showed a decreased width (mean −24%); in the fourth there was a 30% increase.

In the control and angiography groups there were little changes in the clarity of definition of vessel markings. Blurring of vascular markings was seen in one Alloxan-treated dog and two volume-expanded dogs. In no dogs were septal (Kerley) lines seen.

Densitometry

Figure 6A, B show the relationship between extravascular lung water and change in radiographic density for the upper and lower zones. In both upper and lower zones there was a statistically significant relationship between these variables, although there was considerable scatter (upper zone $r=0.45$, $p<0.01$; lower zone $r=0.71$, $p<0.01$). Density changes in control dogs were always less than 20%. The slope of the upper zone relationship was less

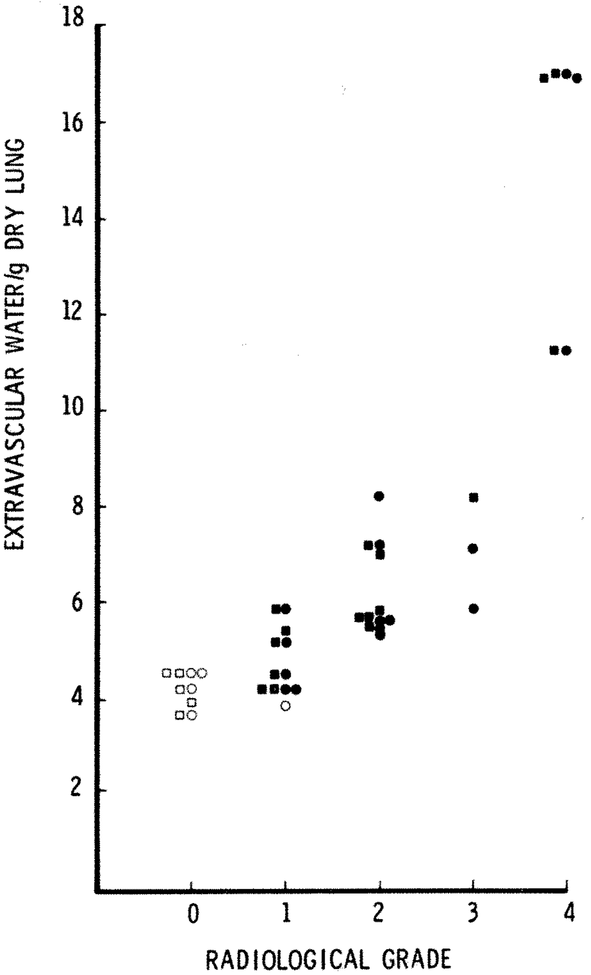


Fig. 5.

Relationship between mean extravascular water/g dry lung of each dog and its highest zonal oedema grade assessed by both radiologists. Control dogs are shown with open symbols oedematous dogs with closed symbols. Radiologist 1 = (○●); radiologist 2 = (□■).

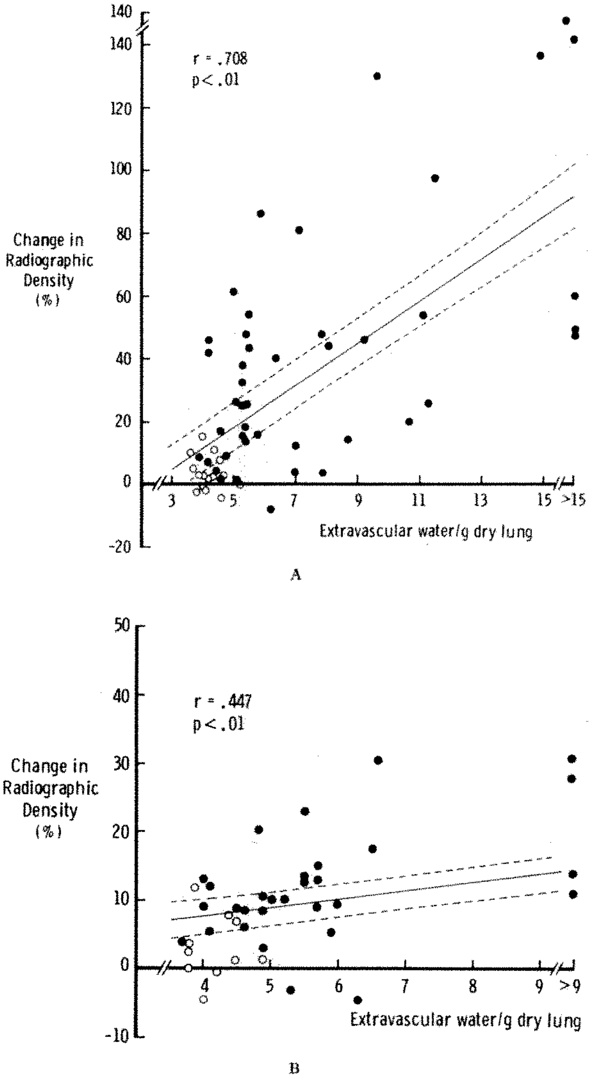


Fig. 6.

Relationship between change in radiographic density and extravascular water in control dogs (○) and oedematous dogs (●). (A) lower zones ($r=0.708$, $p<0.01$). (B) upper zones ($r=0.447$, $p<0.01$). The regression lines (———) and 95% confidence limits (– – –) are shown.

than in the lower zone; thus, in the lower zone a doubling of extravascular water is on average associated with a 40% increase in density, whereas the corresponding increase in the upper zone was approximately 15%. The difference we assume to be due to the differing extent to which extravascular lung water is responsible for the attenuation of the X-rays in these zones. In the upper zones the absolute radiographic density (mean density = 23.1 ± 3.1 mm aluminium) is greater than in the lower zone (mean density = 14.8 ± 2.9 mm aluminium), although the thickness of the lung is less in the upper zones. We assume this high density to be due to the thick muscle layer overlying the upper part of the thorax. Thus, in the upper zone, extravascular lung water is a relatively minor factor in the total X-ray attenuation.

Discussion

This study using direct, gravimetric measurement of lung water has confirmed the findings of Pistolesi and Guintini (1978) that the radiograph is a sensitive method for detecting acute pulmonary oedema. We have found that as oedema develops, radiographs show increased hazy shadowing, and this change was seen in some cases when lung water was still within

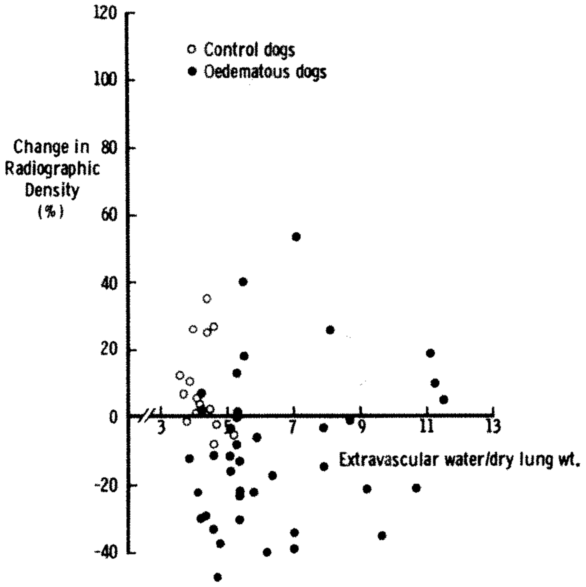


FIG. 7.

Relationship between change in radiographic density and extravascular water. The density values have been adjusted to take account of the decreased area of the radiograph occupied by the lung image after the lung volume has decreased due to oedema. Control dogs (○); oedematous dogs (●).

the normal range. Such early detection, however, was not invariable and in some zones with up to 50% increase of extravascular water, oedema was not detected radiographically. Zonal oedema grades correlated positively with extravascular lung water, although there was considerable overlap between grades. Oedema was detected more easily when there was an associated decrease of lung volume (see below).

A close relationship was seen between the highest zonal grade and mean extravascular water of each dog. This relationship, which is similar in shape to that described by Pistolesi and Guintini (1978) shows that the radiographs become abnormal before lung water is appreciably increased. Thereafter grade and lung water positively correlate. In all cases where extravascular water/dry lung weight ratio was increased by more than 35%, definite oedema was diagnosed. Thus, our results and those of Pistolesi and Guintini suggest that the radiograph is sensitive to the presence of abnormal water and provides a semiquantitative indication of the amount of oedema. Several other studies of cardiogenic pulmonary oedema, using the double-indicator dilution method (Van de Water *et al.*, 1970; Yu, 1971; Fazio *et al.*, 1976) have concluded that the radiograph is less sensitive, becoming positive when extravascular lung water is increased by 30–80%. However, it has been repeatedly demonstrated that the double-indicator dilution technique may overestimate lung water when oedema is due to raised pulmonary vascular pressure (Staub, 1974).

The radiograph is also specific in the sense that radiographs from control dogs were almost invariably recognized as normal when a comparison with base-line films was made. However, without the base-line film a distinction could not be made between mild oedema and normality, and this difficulty was particularly apparent in the upper zones where overlying soft tissue caused confusion. The base-line films were not necessary for the recognition of severe oedema.

The loss of lower zone lung volume was a consistent, though variable feature of pulmonary oedema in this study. When pulmonary oedema occurs in man it is frequently associated with a loss of lung volume, demonstrated radiographically (Kreel and Sandin, 1977) or spirometrically, but there is often doubt as to whether the dyspnoeic patient with pulmary oedema is able to co-operate in taking a deep breath, and this makes the interpretation of this radiological sign difficult. This consideration did did not apply in our study where a constant inflation pressure was used. To the contrary, it is possible that we have minimized the loss of lung volume when we hyperventilated the dogs before taking radiographs since this involved hyperinflation of the lungs and may have temporarily reduced any atelectasis present. In a separate study (Snashall *et al.*, 1980) we have shown that lung volume loss is closely associated with the development of hypoxia due to venous admixture, which suggests that the volume loss is associated with atelectasis or flooding of perfused alveolar units. Atelectasis seems most likely in those dogs with minimal oedema, while flooding with associated volume loss is more likely in the severely oedematous. In volume loaded dogs, an additional factor is the accumulation of a proportion of the infused volume in the abdomen, causing ascites, hepatomegaly and splenomegaly, and forcing up the diaphragm. Other pathophysiological features of pulmonary oedema such as airway narrowing and diversion of perfusion away from the dependent zones occur when the lung looses volume but show little relation to lung water (Snashall *et al.*, 1980). Therefore, by demonstrating loss of lung volume the radiograph may be giving valuable information.

Farney *et al.* (1977) noted a fall in radiographic total lung capacity in man after rapid intravenous infusion of saline. Van Leeuwen *et al.* (1973) found that vital capacity decreased as pulmonary "congestion" developed during saline loading of patients with congestive heart failure. Milne and Bass (1969) found that the abnormally elevated lung volumes (TLC, FRC and RV) of chronic airways obstruction decreased when pulmonary oedema developed.

Although changes in radiographic density correlated with extravascular lung water (Fig. 6), density changes were a poor indicator of the presence of oedema. In many cases large increases in extravascular water were unassociated with any significant increase of density, while in other dogs density was markedly increased with minimal oedema. Density measurement, however, has demonstrated some of the intrinsic problems in the radiographic detection and quantitation of oedema. The relationship between oedema and density is poor because of the varying influence of factors other than increased extravascular lung water. We believe that the most important factors are: (1) lung volume, and (2) pulmonary blood volume.

As oedema develops and lung volume falls, complex changes take place which affect radiographic density unpredictably. At the simplest level, the lung occupies a smaller area of the radiographic image, and density will tend to increase in inverse proportion to the area change. However, correction for area change did not improve the relationship between density and lung water (Fig. 7). Associated with volume loss there are likely to be variable changes in the volume of blood in extra-alveolar vessels, which normally comprises 40–60% of lung weight (Staub, 1974). This volume is a function of lung elastic recoil pressure (Howell *et al.*, 1961); when lung volume is decreased by the diaphragm being pushed up, elastic recoil will diminish and extra-alveolar blood volume decrease; when lung volume decreases due to flooding or microatelectasis, recoil pressure may increase and blood volume also increase. The latter mechanism may predominate in Alloxan-treated dogs, and a combination of mechanisms in the volume-loaded animals. Thus, in Alloxan-treated dogs the width of pulmonary vascular markings tended to increase with oedema, while in volume-loaded dogs with similar degrees of perivascular cuffing and lung volume loss, the width of vascular markings decreased.

Pulmonary angiography with sodium iothalamate (70% w/v) caused a loss of lung volume associated with patchy pulmonary oedema. Chamberlain *et al.* (1979) described pulmonary oedema with normal pulmonary wedge pressure occurring in man after injection of urographic contrast medium. Harrington and Wiedman (1965) demonstrated an increase in vascular permeability of the bat's wing following injection of sodium iothalamate, and other angiographic agents have been shown to increase permeability of cerebral and coronary vessels. Similarly, we believe that the pulmonary oedema was caused by increased endothelial permeability because it developed with normal pulmonary wedge pressure and had a patchy distribution occurring in those zones into which most of the contrast medium had been directed.

If the radiograph detects a 35% increase in lung water, can it be considered an adequate method for the detection of pulmonary oedema? Our study suggests that it is not adequate in all cases. Two out of nine dogs with increases of extravascular lung water of less than 35% developed tachypnoea (mean respiratory rate=34 minute) associated with hypocapnia (mean $PCO_2=14.1$ mm Hg) and hypoxia (mean $PO_2=75.3$ mm Hg). It is likely that this degree of oedma would have greater deleterious effects in old or already diseased lungs, and there is evidence that patients with chronic airways obstruction may be dyspnoeic from radiographically occult pulmonary oedema (Noble *et al.*, 1966). In general, however, the bulk of a 35% increase in lung water accumulates in the extra-alveolar interstitium (Snashall *et al.*, 1977) where its interference with lung function is slight. In general we found a poor relationship between oedema and hypoxia. Frequently severely oedematous dogs had minimal hypoxia. We have investigated the relationship between oedema and gas exchange more fully in a separate study (Snashall *et al.*, 1980).

Can the results of this study be applied to man? In several respects our experiments differ from the clinical situation: the dog's chest is a different shape and usually smaller than that of adult man; we have studied acute oedema, whereas human pulmonary oedema is usually more chronic; our radiographs were taken under highly standardized conditions. In none of these dogs have we observed septal (Kerley B) lines, possibly because of the acute nature of the oedema or due to the poor development of interlobular fibrous septae in the dog. In many respects, however, the radiographic appearances of oedema in these animals was similar to that seen in man and it seems likely that the main effects and appearances of lung oedema will be similar. We believe that sensitivity of the radiograph in the detection of pulmonary oedema in dogs is a guide to its sensitivity in detecting clinical pulmonary oedema.

ACKNOWLEDGMENT

P. D. Snashall was supported by a Senior Fellowship from the Wellcome Trust.

REFERENCES

CHAMBERLAIN, W. H., STOCKMAN, G. D. and WRAY, N. P., 1979. Shock and non-cardiogenic pulmonary edema following meglumine diatrizoate for intravenous pyelography. *American Journal of Medicine*, *67*, 684–686.

FARNEY, R. A., MORRIS, A. H., GARDNER, R. M. and ARMSTRONG, J. D., 1977. Rebreathing pulmonary capillary and tissue volume in normals after saline infusion. *Journal of Applied Physiology*, *43*, 246–253.

FAZIO, F., JONES, T., MACARTHUR, C. G. C., RHODES, R. H., STEINER, R. E. and HUGHES, J. M. B., 1976. Measurement of regional pulmonary oedema in man using radioactive water ($H_2{}^{15}O$). *British Journal of Radiology*, *49*, 393–397.

FISHMAN, A. P., 1976 Clinical disorders of lung liquids. In *Lung Liquids* (Ciba Foundation Symposium) (Elsevier, Excerpta Medica, North Holland) pp. 312.

HARRINGTON, G. J. and WIEDMAN, M. P., 1965. The effect of contrast media on endothelial permeability. *Radiology*, *84*, 1108–1111.

HARRISON, M. O., CONTE, P. J. and HEITZMAN, E. R., 1971. Radiological detection of clinically occult cardiac failure following myocardial infarction. *British Journal of Radiology*, *44*, 265–272.

HOWELL, J. B. L., PERMUTT, S., PROCTOR, D. F. and RILEY, R. L., 1961. Effect of inflation of the lung on different parts of pulmonary vascular bed. *Journal of Applied Physiology*, *16*, 71–76.

KREEL, L. and SANDIN, B., 1977. Chest symposium: the radiology of pulmonary oedema. *X-ray Focus*, *16*, 30–53.

MILNE, E. N. C. and BASS, H., 1969. Roentgenologic and functional analysis of combined chronic obstructive pulmonary disease and congestive cardiac failure. *Investigative Radiology*, *4*, 129–147.

NOBLE, M. I. M., TRENCHARD, D. and GUZ, A., 1966. The value of diuretics in respiratory failure. *Lancet*, *ii*, 257–260.

PEARCE, M. L., YAMASHITA, J. and BEAZELL, J., 1965. Measurement of pulmonary edema. *Circulation Research*, *16*, 482–488

PISTOLESI, M. and GUINTINI, C., 1978. Assessment of extravascular lung water. *Radiologic Clinics of North America*, *16*, 551–574.

SELINGER, S. L., BLAND, R. D., DEMLING, R. H. and STAUB, N. C., 1975. Distribution volumes of ^{131}I albumin ^{14}C sucrose and ^{36}Cl in sheep lung. *Journal of Applied Physiology*, *39*, 773–779.

SNASHALL, P. D., WEIDNER, W. J. and STAUB, N. C., 1977. Extravascular lung water after extracellular fluid volume expansion in dogs. *Journal of Applied Physiology*, *42*, 624–629.

SNASHALL, P. D., KEYES, S. J., MORGAN, B., RAWBONE, R. G., MCANULTY, R. and MITCHELL-HEGGS, P., 1980. Changes in lung volume, perfusion, ventilation and airway diameter in dogs with pulmonary oedema. *Clinical Science*, *59*, 1–11.

STAUB, N. C., 1974. Pulmonary edema. *Physiological Reviews*, *54*, 678–811.

VAN LEEUWEN, A. M., HAVELAAR, W. M. C. and SIMONIS, M. H., 1973. The use of daily measurements of vital capacity in patients with congestive heart failure. *Netherlands Journal of Medicine*, *16*, 155–168.

VAN DE WATER, J. M., SHEH, J. M., O'CONNOR, N. E., MILLER, I. T. and MILNE, E. N. C., 1970. Pulmonary extravascular water volume: measurement and significance in critically ill patients. *Journal of Trauma*, *10*, 440–449.

YU, P. N., 1971. Lung water in congestive heart failure. *Modern Concepts of Cardiovascular Disease*, *40*, 27–32.

Book review

The Practice of Biliary Surgery. By G. A. Kune and A. Sali. pp. xvi+462, 2nd edn., 1980 (Blackwell Scientific Publications, Oxford), £32·50.
ISBN 0–362–00589–0.

Here is a fine book whose sections on imaging and therapeutic radiology are written by authors of the excellence of Hiram Baddeley and Joachim Burhenne. The main authors are a Professor of Surgery and his first assistant at the University of Melbourne. The book covers all aspects of biliary disease, proceeding logically through sections on biliary anatomy, physiology and radiology to more specialized chapters on the management of benign biliary strictures and acalculous benign biliary disease. The text is especially economical with large print size and generous spacing. It is illustrated with well selected radiographs with the addition of many elegant yet simple line drawings. This makes each chapter a pleasure to read and engenders a "please-read-on" frame of mind during reading. The book is best suited for the clinical surgeon, though it is obvious in all chapters that modern biliary surgery could not function without up-to-date radiology. The radiologist will find interest in all chapters including those on hepato-biliary hydatid liver disease and paediatric biliary disease. I would criticise the excessive number of references, the chapter on gall-stones boasting 380 and consuming 15 pages. Surely only key references would suffice.

In summary, this is an updated, concise coverage of the biliary system which is of interest to radiologists though not an essential buy.

R. DICK.

1981, *British Journal of Radiology*, 54, 289–295

A method of measuring the radio-opacity of catheters

By J. C. Gore, Ph.D. and G. R. Hooker, D.C.R.(R)

Department of Medical Physics, Royal Postgraduate Medical School and Hammersmith Hospital, London W12 0HS

(*Received December 1979 and in revised form September 1980*)

ABSTRACT

Two methods for measuring the radio-opacity of catheters are described. An analysis of the physical quantities that are important for the satisfactory detection of a catheter inside a patient shows that an intrinsic index of radio-opacity can be defined and measured using a radiograph of a step wedge. Quantitative comparisons between catheters of different compositions may then be made, and results are presented of measurements made on several commercially available devices. It is suggested that the methods described are more satisfactory than previous techniques used to define standards, and that they highlight some anomalies in current catheter design and usage.

A wide variety of catheters and tubes is currently used for diverse purposes in radiological procedures; one of the important factors affecting the suitability of a catheter for any such purpose is its radio-opacity, since this determines the ease and accuracy of locating the catheter inside a patient. It is, however, not usual for manufacturers to describe the relative radio-opacities of catheters in anything but the vaguest qualitative terms, so the choice of catheter has to be made in ignorance of its likely perceptibility on an X-ray image. A contributory factor to this situation has been that, to date, there has been no satisfactory, generally accepted method for quantitatively measuring the opacities of catheters, or any satisfactory criteria by which their radio-opacity may be assessed. We present here a simple method of quantitatively measuring catheter opacities and use it to assess several catheters in current use, in the hope that it will stimulate a more rigorous approach to the description of radio-opacity.

The radio-opacity of a catheter may be defined in terms of its fractional absorption of X rays, but there are several other factors that affect the perceptibility of a catheter when it is irradiated inside a patient and its shadow is recorded on an image intensifier or film. It is essential therefore to distinguish between the intrinsic opacity of the catheter, which should be defined in a manner independent of any particular method of measurement, and its actual perceptibility in practical situations, although criteria for acceptance as radio-opaque may be largely based on measurements of the ease of detection in realistic conditions. The analysis below shows how some of the different factors that affect perceptibility are interrelated, and a method of measuring radio-opacity is then described.

PRINCIPLE OF THE METHOD

The principle behind the method relies on the postulate that a radiograph of a catheter can be produced which is limited only in contrast, *i.e.* in which the image may be recorded but is not perceived by reason only of its low contrast, so that no improvement in the recording resolution, or reduction in image noise, will improve the likelihood of detecting the catheter. The rationale of this method is illustrated by considering a simple experiment in which several radiographs are taken of a catheter using different exposures, producing images of the catheter recorded on different background film densities. After viewing by eye, it will be found that the catheter can be seen only in some of the radiographs but not in the others, because in some of the films the image contrast falls below the threshold contrast necessary for detecting the catheter. The catheter possesses an intrinsic radio-opacity which produces a radiation contrast at the film, but the translation of this radiation contrast into differences of visible light at the eye depends upon the characteristic curve of the recording system. For a radiograph, the characteristic or Hurter-Driffield curve displays the variation of film density with the logarithm of exposure, and for moderate film densities the gradient of this curve increases continuously with exposure, so that at any film density a local gradient, γ, may be defined (Fig. 1). The analysis below suggests that we may define an intrinsic radio-opacity index, ρ, such that, in restricted circumstances,

$$\rho = \frac{k}{\gamma_{\min}} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k is a constant and $\gamma_{\min}$ is the threshold value of the slope of the characteristic curve at which the contrast obtained can just be perceived; when the slope is less than $\gamma_{\min}$ the image is usually not seen because the contrast is too low, whilst above this value the image is usually detected. The method described essentially involves estimating ρ from measurements of $\gamma_{\min}$.

Physically $\gamma_{\min}$ corresponds to a measure of the enhancement of the radiation contrast of the catheter, provided by the recording film, needed to produce a detectable image. The intrinsic radio-opacity index,

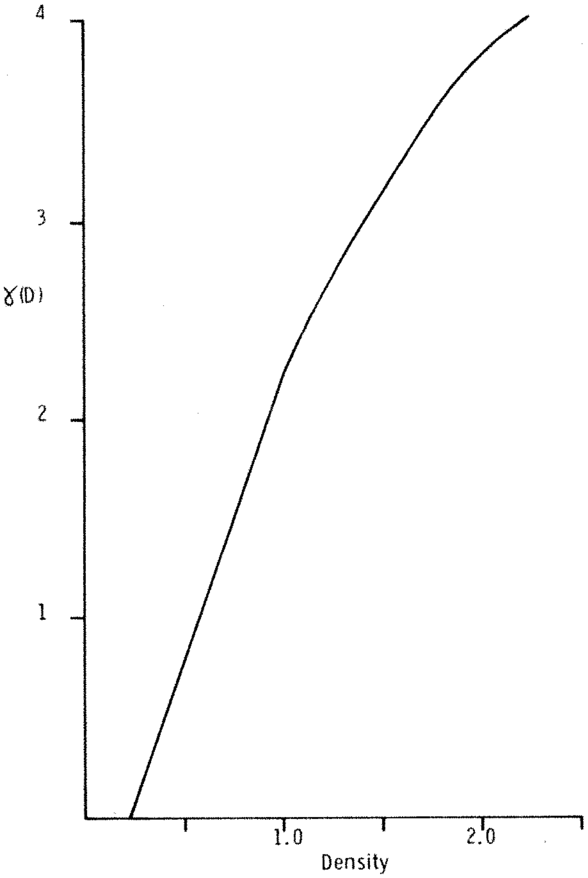


FIG. 1.

Variation of slope of characteristic curve, γ, with film density for typical non-screen X-ray film.

ρ, can therefore be determined by observing the slope of the characteristic curve at the density at which the catheter becomes detectable. Varying the film exposure will produce radiographs of different densities corresponding to different portions of the characteristic curve, with different slopes. The validity of equation (1) may be established by calculating the expected contrast of a catheter image.

CALCULATION OF THE IMAGE CONTRAST

Consider a catheter of external radius R and internal radius r, composed of material that has a linear attenuation coefficient μ. When exposed in air, the shadow of this catheter produces a variation of X-ray exposure at the film $I(x)$, where x is the distance from the mid-line of the shadow,

$$\begin{aligned} I(x) &= I_0 \exp(-2\mu[(R^2-x^2)^{\frac{1}{2}}-(r^2-x^2)^{\frac{1}{2}}]) \; (x<r) \\ &= I_0 \exp(-2\mu(R^2-x^2)^{\frac{1}{2}}) \; (r<x<R) \\ &= I_0 \; (x>R) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2) \end{aligned}$$

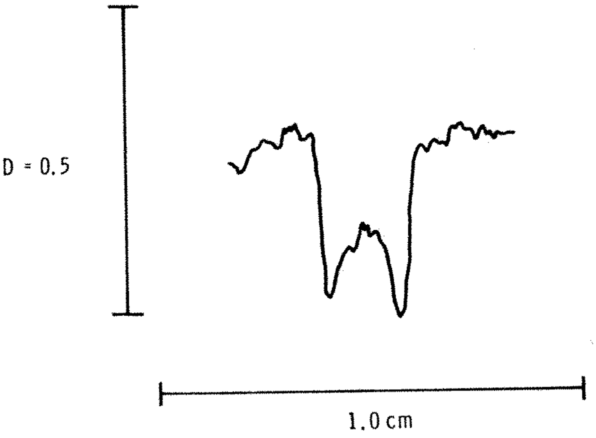


FIG. 2.

Microdensitometer trace through image of a catheter, showing typical density profile, $D(x)$.

where I_0=the exposure to the film outside the shadow of the catheter.

When the catheter is placed on a scattering medium such as a step wedge, then at the film there is also present scattered radiation of intensity SI_0, which can be considered uniform over distances of the order of the size of the catheter.

We further assume, with no loss of generality, a parallel X-ray beam, so that the magnification is unity, and negligible recording unsharpness, achievable in practice by using a large film–focus distance, fine focal spot, and non-screen film.

The variation of X-ray exposure, $I(x)$, produces a variation in density, $D(x)$, on the film which will in general have a profile of the form shown in Fig. 2, a microdensitometer trace through the image of a catheter. If the film density is related to the common logarithm of the exposure as

$$D(x)=f(\log I(x)) \quad . \quad . \quad . \quad . \quad (3)$$

then f describes the shape of the characteristic curve of the film. The minimum density occurs at a distance $x=r$ from the mid-line of the catheter, where the exposure is $I_{\min}$.

$$I_{\min}=I_0(S+\exp(-2\mu(R^2-r^2)^{\frac{1}{2}}) \quad . \quad (4)$$

whilst $I_{\max}=I_0\,(S+1)$ is the exposure to the film background.

The density produced by $I_{\min}$ is $D_{\min}$, which may be estimated by a Taylor expansion. If the background film density is $D_{\max}$

$$D_{\max}=f(\log(S+1)I_0) \quad . \quad . \quad . \quad (5)$$

By expansion of f around $D_{\max}$, ignoring terms of second order and above, we obtain

$$D_{\min}=f(\log(S+1)I_0+\log\left(\frac{S+\exp(-2\mu(R^2-r^2)^{\frac{1}{2}})}{S+1}\right)\left.\frac{\mathrm{d}D}{\mathrm{d}(\log I)}\right|_{D_{\max}} \quad (6)$$

It is readily shown, from Fig. 1, that the second term is typically some 50 times greater than the third or subsequent terms, so the truncation of the expansion is justifiable. Thus, for low contrast objects, the maximum difference in density, $\varDelta D$, is

$$\varDelta D=\gamma(D_{\max}).\frac{\exp(-2\mu(R^2-r^2)^{\frac{1}{2}})-1}{S+1}.\log_{10}e \quad (7)$$

where $\gamma(D_{\max})$ = the gradient of the D vs. $\log I$ curve at $D_{\max}$ and second and higher order terms in the expansion of the logarithmic expression have been ignored. The percentage visual contrast, C, is conventionally defined (Farrell and Booth, 1975) in terms of the difference in light intensity received at the eye.

$$C=100\left|\frac{10^{-D_{\max}}-10^{-D_{\min}}}{10^{-D_{\max}}+10^{-D_{\min}}}\right|\%$$

$$\simeq\frac{100\gamma(D_{\max})\mu(R^2-r^2)^{\frac{1}{2}}}{(S+1)}\% \quad . \quad . \quad . \quad (8)$$

No loss of generality is introduced by our particular definition of contrast in terms of the maximum variation of luminance across a somewhat irregular shape. Such a choice accords with conventional descriptions of visual stimuli, and it serves as a convenient parameter to describe the luminance scale of the catheter image.

THE DETECTION PROCESS

Equation (8) relates physical properties of the catheter to a visual stimulus, C, which will determine whether the catheter is seen. To be able to detect the catheter, the visual system requires this contrast to exceed the threshold contrast for an object of this size under normal viewing conditions. The postulate that such a threshold exists and can be determined is well substantiated by psychophysical experiments, although more complex models of perception suggest that no sharp threshold exists, but that the probability of detection of the catheter increases continuously with C, so that we should really postulate that the probability of detection depends on the quantity given by equation (8). In practice, we find the threshold to be adequately sharply defined so that, to be detected at all, the contrast C must exceed a threshold value C_{T} measurable with reasonable precision. However, our results could equally be expressed in terms of a detection probability.

The threshold contrast, C_{T}, will itself depend on a number of factors. It will vary with the viewing conditions, and in particular the luminance of the image and the distance of viewing. However, it is not unreasonable to suppose that the contrast sensitivity of the eye when viewing the catheter profile will show a behaviour similar to the response of the eye to intensity variations resulting from sine and square wave gratings, or other simple shapes (Farrell and Booth, 1975; Overington, 1976), and thus it will not vary significantly from observer to observer (if all observers have visual defects corrected) nor over the variations of luminance of viewing boxes that might arise in practice. In general, the threshold contrast of the eye varies quite considerably with luminance at low light levels, but under normal conditions of viewing radiographic illuminators, the eye is exposed to luminances of the order of 10–500 cd/m^2 and, under these photopic conditions, the contrast sensitivity of the eye remains constant even for large variations in light level (Overington, 1976, p. 50). However, the threshold contrast will depend on the angle, α, subtended by the image at the eye, so we should write $C_{\mathrm{T}}(\alpha)$. Since α will usually be $\ll 1$ radian, we may write $\alpha=2R/d$ (or, if each side of the catheter is perceived individually, $(R-r)/d$), where d = the distance of viewing. Furthermore, in situations where the magnification factor, m, is greater than 1, to a good approximation the profile is simply scaled linearly so that the image subtends an angle $2mR/d$. Thus, as a condition that the catheter be seen, we may write that the catheter contrast in equation (8) should exceed the threshold contrast for an image of the relevant angular size:

$$\frac{100\gamma(D_{\max})\mu(R^2-r^2)^{\frac{1}{2}}}{S+1}\geqslant C_{\mathrm{T}}\left(\frac{2mR}{d}\right) \quad . \quad . \quad (9)$$

Equation (9) summarizes the necessary conditions for detecting a catheter. The exact form is determined to some extent by our choice of definitions and model of perception, but any other realistic choice would produce a similar expression. It is clear that the greater the catheter thickness, and the more attenuating the material, the more readily will it be detected. In many clinical situations S is large and the detectability of the catheter depends critically on the radiographic technique. For example, Dick *et al.* (1978) quote values for S ranging between 2.5 and 6.5 when the distance between patient and film is varied from 25 to 0.3 cm, and the product of patient thickness and beam diameter is 500 cm^2. The reduction of S, by using small fields, low kV and anti-scatter grids, will significantly aid catheter detection. Furthermore, whilst the general shape of C_{T} is reasonably constant for most observers, the choice of m and d will determine the region of the contrast sensitivity curve on which any one catheter falls. In practice, at a fixed viewing distance, C_T generally increases as mR/d decreases. However, if we allow an observer to optimize his viewing conditions by changing his eye–film distance, then by suitable choice of d he can ensure that all catheters are viewed at the minimum value, C_T (min). It is interesting to note that if the viewing conditions are fixed, different sized catheters will be detectable at different levels of the observer's contrast sensitivity, in which case the threshold contrast required for any catheter to be detected is related to its size.

Methods of Measuring Radio-opacity

Equation (9) shows that the factor $\mu(R^2-r^2)^{\frac{1}{2}}$ uniquely determines the intrinsic radio-opacity. At threshold,

$$\mu(R^2-r^2)^{\frac{1}{2}}=\frac{C_T(\min)\,(S+1)}{100\gamma\,(D_{\max})} \quad . \quad . \quad (10)$$

In principle, therefore, this intrinsic characteristic could be estimated from measured values of C_T, S and γ. Indeed, a straightforward method of determining relative radio-opacities is suggested by equation (7). The maximum density differences, ΔD_1 and ΔD_2, produced by two catheters radiographed to give similar background densities, can be related to each other by expanding the exponential function in equation (7) to obtain

$$\frac{\Delta D_1}{\Delta D_2}=\frac{\mu_1(R_1^2-r_1^2)^{\frac{1}{2}}}{\mu_2(R_2^2-r_2^2)^{\frac{1}{2}}} \quad . \quad . \quad . \quad (11)$$

Thus, if the second catheter is a standard to which all others are to be compared (it could, alternatively, be a thin aluminium rod), then relative radio-opacities may be estimated by careful measurements from radiographs, using a scanning microdensitometer. This procedure would not be simple for many users, although such a method might be suitable for standardization purposes. However, a psychophysical method is suggested by equation (10) which would be more suitable for measurements by potential users. We may regard γ as a variable such that, for a given catheter and fixed S and C_T, its value determines whether the catheter is seen.

Using the fact that at low densities γ generally increases monotonically with density (Fig. 1), then if a catheter is radiographed on top of and aligned with an aluminium step wedge, each step effectively produces a separate image with its own value of exposure, density, and therefore γ. The use of a step wedge provides a convenient method of producing the equivalent of many different exposures on a single film. The catheter will not be seen on those steps of the wedge for which γ is less than the critical value, $\gamma_{\min}$. The gradient of the characteristic curve of the film at the density corresponding to the step on which the catheter is just seen is, from equation (10), directly related to the intrinsic radio-opacity.

A simplified practical method

In practice, no separate measurement of the characteristic curve is necessary if the step wedge is suitably constructed so that each step further reduces the intensity of the X-ray beam by a constant factor. Heterogeneous X-ray beams undergo beam hardening in absorbers, with the result that the intensity of an X-ray beam does not decrease exponentially through an aluminium block. However, an approximately exponential decrease of intensity with absorber thickness with little change in beam quality can be obtained with a beam that has been suitably filtered, which then passes through an aluminium step wedge, and exits through a thin (0.5 mm) copper filter which removes soft and scattered photons (Corney and Seemann, 1947). The measured behaviour of a 70 kV beam is shown in Fig. 3. For such a step wedge, the exposure to the film is given by

$$I_n=I_1\exp(-\mu_a(n-1)t) \quad . \quad . \quad . \quad (12)$$

where t=the thickness of each step; n=the step number; I_1=the exposure through step 1; μ_a=the *apparent* linear attenuation coefficient of the wedge. Thus:

$$\log I_n=\log I_1-\mu_a(n-1)t\log e$$

In place of the true film characteristic curve, therefore, we may substitute the curve of density against step number, and simply note that

$$\gamma=\frac{dD}{d(\log I)}\simeq\frac{\log_e 10}{\mu_a t}\,\frac{\Delta D}{\Delta n} \quad . \quad . \quad . \quad (13)$$

where ΔD is the difference in density between two steps that differ in thickness by $t\Delta n$. In particular, the density difference, $\Delta D'$, between two steps numbered $(n-1)$ and $(n+1)$ is related to the gradient of the characteristic curve, γ, by,

$$\Delta D'=\frac{\gamma\mu_a}{\log_e 10}\cdot 2t \quad . \quad . \quad . \quad (14)$$

If the image of the catheter disappears on the step numbered n, then γ takes the minimum value needed to render the catheter just visible. From equation

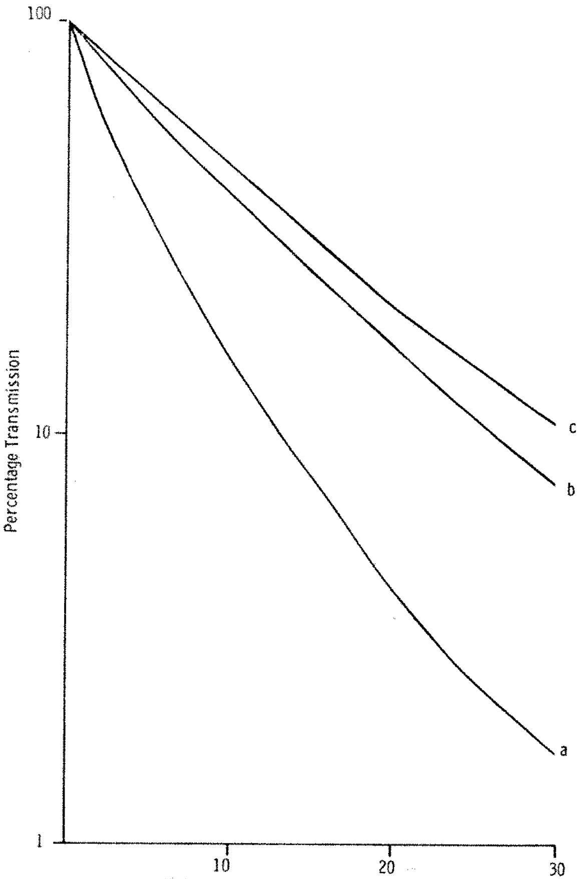


FIG. 3.

Attenuation of heterogeneous X-ray beams in aluminium. Measurements were made of the per cent transmission of a beam generated at 70 kV, and a curve of the form $\log(100.I/I_0)=A-Bx-Cx^2$ (x in mm) was fitted by the method of least squares, so that the value of C indicates the extent of deviation from truly exponential attenuation, whilst $B=\mu_a \log_{10}e$ (see text). (a) Aluminium alone. $A=1.98$, $B=0.0808$, $C=0.0008$. (b) Aluminium with 0.5 mm copper filter added below. $A=2.00$, $B=0.0435$, $C=0.0002$. (c) Aluminium with 0.5 mm copper and 30 mm aluminium added below. $A=1.99$, $B=0.0361$, $C=0.0001$.

TABLE I

RESULTS OF MEASUREMENT OF RADIO-OPACITY INDEX

Catheter	Radio-opacity index
Ureteric catheter Portex red 3FG 300/500/030	53
Deseret epidural	53
Portex blue line infants feeding tube 400/220/040 4FG	53
Wallace epidural	53
Deseret E–Z catheter 2236 R/O. 14GA	58
Centrasil infusion cath. 2N1510 VS868 16G	63
Bard 1 cath. 14G U185895 1814	63
Vygon pediatric duodenal catheter FG5 2395.05	63
Deseret E–Z cath. radiopaque	67
Vygon Longline Surcath. 17317	67
Bard 1 cath. 1617 R intravenous catheter	72
Portex epidural cannula 100/380/500 R/opaque	76
Centrasil introducer 3 in.	80
Vygon De Lee suction catheter FG5	83
Sherwood ubilical artery catheter MAR1602 FG5	83
B.D. Longdwel IV catheter needle 16G8	87
Travenol Vicra Centrasil 16G	90
H. G. Wallace 15% bismuth (yellow)	91
Vygon infant feeding tube FG6 (31006)	93
Sherwood feeding tube MAR1612 CH3.5	93
H. G. Wallace 12% barium FEP (white)	100
Deseret E–Z catheter plain	117
Vygon Levin duodenal tube FG14	135
Portex epidural cannula 100/380/040 R/opaque	135
Edwards Lab. Swan Gantz triple lumen catheter	135
Deseret E–Z cath. 2034 16 gauge	142
Sherwood intramedicut B	150
Deseret E–Z cath. 2032 18GA	150
Vygon silicon catheter 2180.20	150
Abbott drum cartridge catheter 4719 14G radio-opaque central venous catheter	175
Sherwood Levin stomach tube MAR2650–12 CH12	175
Sherwood intramedicut	195
Portex tubing	200
Vygon Ryle tube (with metal olive) FG16 ORX392/6	200
Braun cavafix with radiopaque stylet	200

(10), with the effects of any residual scatter incorporated into the definition of the effective attenuation μ_a, we obtain

$$\mu(R^2-r^2)^{\frac{1}{2}}=\frac{C_T(\min)\,2.\mu_a t}{100.\log_e 10.\Delta D} \quad . \quad . \quad (15)$$

Clearly, the ratio $2t/\Delta D$ is directly related to the intrinsic radio-opacity and is readily determined with the aid of a densitometer when the step heights are known. We therefore refer to this ratio as the Radio-opacity Index, ρ, when t is measured in mm.

$$\rho=\frac{2t}{\Delta D}=\frac{\mu(R^2-r^2)^{\frac{1}{2}}.100.\log_e 10}{C_T(\min)\mu_a}=\frac{k}{\gamma_{\min}}. \quad (16)$$

The procedure envisaged for measuring ρ is that sufficiently long test specimens are placed on top of an aluminium step wedge and copper filter in the middle of a non-screen X-ray film, positioned on a thin (2 mm) sheet of lead. The step wedge should have a thickness range from 30 to 80 mm in steps of 3 mm or less and each step should be 10 × 100 mm in area. The catheter and wedge are then simultaneously irradiated with X rays at 70 kV, with a film–focus distance of at least 1 m. The X-ray quality must be standardized to ensure that μ_a is fixed, and we suggest that the method of Ardran and Crookes (1968) be used to measure the effective kV. Inspection of the image enables the thickness of aluminium

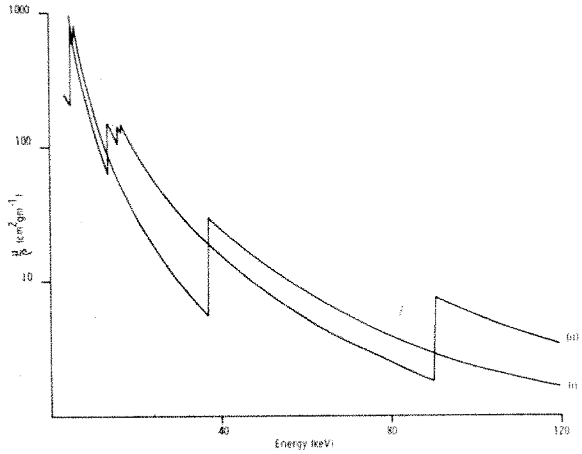


Fig. 4a.

Variations with energy of the mass-attenuation coefficients, μ/ρ, of (i) barium, (ii) bismuth.

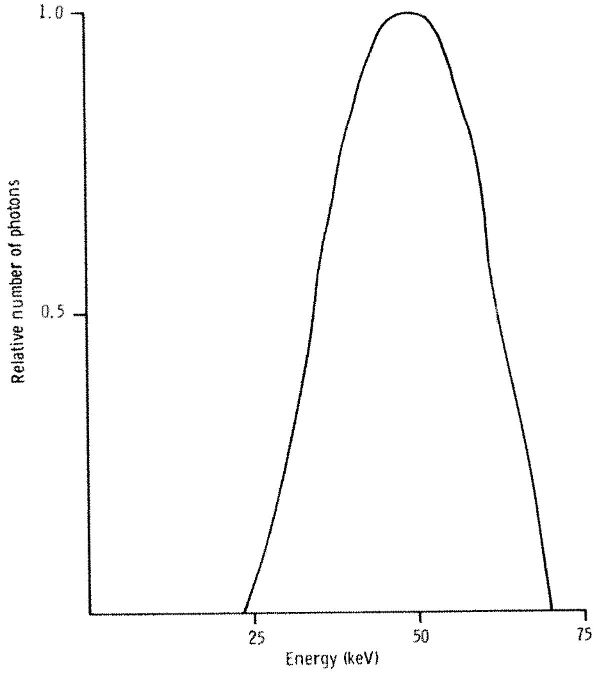


Fig. 4b.

Distribution of photon energies in spectrum of beam generated at 70 kV and filtered by 15 cm tissue, with no scatter.

through which the image is just recognizable to be determined. The densities of the steps adjacent to this transitional step are measured, and the lower density is subtracted from the higher density. This difference in density is divided into the difference between the thicknesses of the two steps to give ρ.

Practical Results

The method has been used to measure the ρ values of sundry commercially available tubes and catheters. The results are shown in Table I. It will be seen that the measured indices cover a considerable range, and that even amongst catheters of similar construction and application there is wide variation. The measurements do not correlate well with the manufacturers' descriptions, *e.g.* some "plain" catheters are more radio-opaque than those specifically labelled as such. Furthermore, these measurements show that the relative opacities of catheters doped with heavy elements accord with the values expected from considerations of the X-ray attenuation coefficients of the added material. For example, a 12% barium catheter appears more opaque than a 15% bismuth catheter, even though barium (atomic number 56) might be expected to absorb less efficiently than bismuth (atomic number 83). However, Fig. 4a shows the variations with energy of the mass-attenuation coefficients for barium and bismuth, whilst Fig. 4b shows the photon spectrum emitted by a tube operating at 70 kV, filtered by 15 cm tissue (Birch *et al.* 1979). Since the K edge of bismuth is at 90.5 keV, whilst that of barium is at 37.4 keV, the mass attenuation coefficient of barium exceeds that of bismuth over most of the useful range of the photon spectrum. This result indicates not only that the proposed method gives sensible results, but also that the relative opacities may well vary with beam quality. This expected variation implies that a complete description of catheter opacity requires measurements at different beam qualities, and the method described can be suitably adapted.

Radiographs have also been made with the catheters in a scattering medium (a water bath, 20 × 20 × 15 cm). The catheter images were viewed and rated subjectively, and those for which ρ was less than 70 were considered to be very difficult to see under these realistic conditions, whilst those that rated greater than 100 were generally seen quite easily. Thus, the index correlates well with subjective assessments of opacity, and it would seem that ρ should be of the order of 100 or more for a catheter to be visible under realistic conditions. When $\rho = 100$, assuming $R = 0.8$ mm, $r = 0.5$ mm, $S = 4$, $C_T(\text{min}) = 1\%$ and $\mu_a = 0.083$ mm^{-1}, then μ needs to be ~ 0.058 mm^{-1} for the catheter to be seen. This corresponds, for a 70 kV beam filtered by several centimetres of tissue (mean energy approximately 45 keV), to a material whose linear attenuation coefficient is midway between soft tissue ($\mu \simeq 0.024$ mm^{-1}) and cortical bone ($\mu \simeq 0.092$ mm^{-1}) (data taken from Birch *et al.*, 1979). It is instructive to calculate the expected ρ values for commonly used materials. For example, assuming that μ for polythene decreases from 0.0207 mm^{-1} at

40 keV (corresponding to a typical mean beam energy) to 0.0180 mm^{-1} at 60 keV, the expected values of ρ for our typical catheter, making our previous assumptions for R, r, C_T and S, decrease from 36 to 31, indicating that a polythene catheter of this size would not be detectable. However, the necessary value of μ of 0.058 mm^{-1} can be achieved by adding barium. For a catheter of this size, the requisite percentages of barium to be added are respectively 9.3, 2.3, 4.2 and 6.7% for 30, 40, 50, and 60 keV monoenergetic beams.

It is also instructive to consider existing standards for radio-opacity, such as the American Veterans' Administration Specification X-1371e for catheters, the American Society for Testing and Materials (ASTM) standard (developed by an ASTM Task Force on Radio-opacity), and a recent draft standard of the British Standards Institution (BSI Document 78/61379). In all these methods, no allowances are made for the effects of the film response on the perceptibility of catheter images. A catheter is radiographed aligned on an aluminium step wedge, so that the film beneath 10 (or 16) mm of aluminium is exposed to density 1. The acceptance criterion is that the catheter should be clearly discernible beneath a thickness of aluminium of not less than 10 (or 16) mm. Of course, none of these standards measure true catheter radio-opacity, since the result obtained depends crucially on the radiographic conditions and particularly on the characteristic of the film used to record the image, and it is doubtful whether any conclusion about a catheter's opacity can be made by this technique. Furthermore, to be acceptable according to these standards, a catheter must be discernible on a film exposed under conditions of little scatter, to density 1, so that for most commonly-used X-ray films the catheter image falls on a region of the characteristic curve for which γ takes a value in the range 2 to 3. Thus, according to these standards, substituting into equations (13) and (16), catheters are acceptably radio-opaque when $\rho > 14$ ($\gamma = 2$) or 9 ($\gamma = 3$). Our experiments suggest that this is too small to be acceptable in realistic conditions, especially where a high scatter/primary ratio at the film degrades the image.

The analysis and measurements above indicate that the perceptibility of a catheter in a radiograph is dependent on several factors, including not only the intrinsic properties of the catheter but also the choice of operating conditions of the X-ray system and the geometrical arrangement of the catheter, patient and film. Such variations should be borne in mind when drawing up acceptance criteria for catheters, and they help to explain why different users have varied opinions of the acceptability of the same catheter.

ACKNOWLEDGMENTS

We thank Professors J. S. Orr and F. H. Doyle for their useful criticisms, Dr. J. V. Farman and Mr. H. G. Wallace for introducing us to the work, and Mr. R. Stockley for providing the catheter samples.

REFERENCES

ARDRAN, G. M. and CROOKS, H. E., 1968. Checking diagnostic X-ray beam quality. *British Journal of Radiology*, *41*, 193–198.

BIRCH, R., MARSHALL, M. and ARDRAN, G. M., 1979. *Catalogue of Spectral Data for Diagnostic X-rays* (Hospital Physicists' Association, London).

CORNEY, G. M. and SEEMANN, H. E., 1947. A logarithmic step tablet for X-rays. *Nondestructive Testing*, *6*, 277.

DICK, C. E., SOARES, C. G. and MOTZ, J. W., 1978. X-ray scatter data for diagnostic radiology. *Physics in Medicine and Biology*, *23*, 1076–1085.

FARRELL, R. J. and BOOTH, J. M., 1975. In: *Design Handbook for Imagery Interpretation Equipment* (Boeing Aerospace Company, Seattle, USA).

OVERINGTON, I., 1976. *Vision and Acquisition* (Pentech Press, London).

Book review

Roentgenologic Anatomy: an Introduction. By W. Frik and U. Goering, pp. 138, 1980 (YB Medical Publishers, Chicago/London; Thieme, Stuttgart), £6·75.
ISBN 0-8151-3292-1.

This neat pocket-sized book, translated from the German, is intended primarily for X-ray technicians, engineers and chemists, and presents anatomy at a very basic level. The aim was obviously to keep the book very small with a strong flexible cover so that it might be carried around. The book contains a very brief introduction to medical terminology, radiation physics and imaging methods, followed by the anatomy of the skeleton and systems in only 60 small pages. This is illustrated by clear diagrams and has a paragraph at the end of each section explaining the radiological demonstration of the organs described. This is followed by a summary of special investigations and positioning. The terminology contained in this section and the chapter on radiation hazards and protection could be of value to the ward nurse who is preparing patients for X ray. The last part of the book consists of a series of most beautifully reproduced radiographs showing typical normal appearances of most parts of the body.

As an introduction for radiography students in their first few weeks of training, this little book could usefully be included in the School of Radiography library. It would be of use to Medical Secretaries in the X-ray Department.

J. DAVIDSON.

1981, *British Journal of Radiology*, 54, 296–301

Left ventricular segmental wall motion—a comparison between equilibrium radionuclide angiography and contrast angiography

By *D. N. F. Harris, M.B., D.A., †D. N. Taylor, M.Sc., *B. C. Ogilvie, M.R.C.P., F.R.C.R., †N. W. Garvie, M.Sc., M.R.C.P., F.R.C.R., *J. Watkins, M.R.C.P., †D. M. Ackery, M.A., M.B., M.Sc. and †N. Conway

*Wessex Cardio-thoracic Unit, Southampton and
†Wessex Regional Department of Nuclear Medicine, Southampton

(Received January 1980 and in revised form June 1980)

Abstract

The qualitative assessment of left ventricular wall motion using a four-point scale has been compared between left ventricular contrast angiography and equilibrium radionuclide angiography in the 30° right anterior oblique projection. Analysis was carried out for five segments of the left ventricle. Four modes of analysis of equilibrium radionuclide angiography were compared and the reproducibility assessed. Overall accuracy of equilibrium radionuclide angiography compared to contrast angiography was greater than 82% to within one degree of motion. One method, using a cine display, averaged 97%. We suggest that equilibrium radionuclide angiography using the cine display is the non-invasive investigation of choice in the screening of patients with suspected regional wall motion abnormalities.

Radionuclides can be used to give a simple non-invasive assessment of ventricular function. In this paper we compare the qualitative assessment of left ventricular wall motion between equilibrium radionuclide angiography and single plane left ventricular contrast angiography. Both investigations were carried out in the 30° RAO projection. Several authors (Zaret *et al.*, 1971; Burow *et al.*, 1977), have stated that there is good correlation between the two methods, but there is a lack of information on the accuracy with which any given segment of the left ventricle can be seen. In particular (Pierson *et al.*, 1977), the accuracy with which movement in the diaphragmatic segments can be seen has been questioned.

LAO equilibrium radionuclide angiography is widely used as there is no overlap between left and right ventricles in this view. However, the LAO view is rather less good, on its own, than the RAO view for detecting abnormalities of regional wall motion. Combining the two views should offer the most accurate assessment of regional wall motion, if the RAO view, using equilibrium studies, can be shown to be accurate.

In this study analysis was carried out for five recognized segments of the left ventricle, excluding the valve planes. Four modes of analysis of equilibrium radionuclide angiography were compared, and the reproducibility assessed.

Materials and Methods

Fifty unselected patients who had undergone contrast angiography for assessment of angina (22), valvular disease (28) or heart failure (8) were investigated by radionuclide angiography within five days of catheterization; some patients had more than one diagnosis. Thirty-two were male, 18 female; age range 20–76 (mean 45). There had been no change in symptoms or medication between the two investigations. Patients were entered into the study by a cardiologist who took no part in the subsequent analysis of results. The criterion for satisfactory contrast angiography was a good contrast bolus followed by three normal ventricular contractions.

Thirty-six patients were included for the final analysis of the two techniques. The grounds for rejection for the other 14 patients were unsatisfactory contrast angiography (9), unsatisfactory radionuclide technique (3), and ectopic contraction rate of greater than one in ten (2).

After premedication (Diamorphine 2.5 mg and Perphenazine 25 mg, or Lorazepam 2 mg) routine contrast angiography was performed. The next day radionuclide angiography was carried out using *in vivo* erythrocyte labelling and a Searle LFOV gamma camera* interfaced to a MDS† Trinary computer (32 K). Ten μg/kg of stannous pyrophosphate (10) were injected intravenously, followed 20 minutes later by 740 MBq (20 mCi) of $^{99}Tc^{m}$ pertechnetate. The patient was placed supine, with the camera in the 30° RAO projection, and three electrodes attached to the chest wall, positioned to give a precisely defined R wave on the electrocardiographic monitor, avoiding the cardiac region of interest. The upstroke of the R wave was used to generate a pulse to signal the beginning of each cycle of data acquisition. Using the display on a storage oscilloscope the camera was positioned to be orthogonal to the long axis of the left ventricle; when the heart and count rate were stable acquisition was begun.

---

*Medium energy high sensitivity collimator.
†Medical Data Systems (International), Dublin, Eire.

The mean heart rate was displayed every ten heart beats; when it was stable, the computer was instructed to divide the last displayed heart rate by 28 and take that time interval as the time/frame for the study.

Each cardiac cycle was divided into 28 frames, and not less than 250000 counts per frame acquired, over 10–20 min.

The assessment of left ventricular wall motion by both contrast angiography and radionuclide angiography were scored on a four-point scale; 0=good movement, 1=hypokinesia, 2=akinesia, 3=dyskinesia.

Routine assessment of wall motion was made from the left ventricular angiogram (by a single observer).

Computer analysis of radionuclide studies

Four analytical methods were used. One method showed a cine display of the whole image, using each of the 28 frames of the cardiac cycle. The remaining three methods used the derivative of the spatial distribution of counts, on diastolic and systolic frames only, to determine wall motion. Standard nine-point smoothing operations were used throughout, the number of smooths being given in the text.

Cine display

This method used a real-time endless-loop flicker-free cine display of the intra-cycle cardiac frames (called FINE on the MDS computer system). Each frame of the 28-frame cycle was smoothed once. The frames were then normalized to a constant maximum, based on the end-diastolic left ventricular maximum counts, to avoid a false impression of motion due to a varying ratio of counts between the left ventricle and the background. The frames were then packed into buffers with background subtraction of between 20 and 30%, chosen subjectively to improve definition of the aortic valve plane. No difference in wall motion was seen over this range.

The complete cardiac cycle was viewed in monochrome as a cine display.

Edge detection

The 28 frames were viewed sequentially to determine end-systole. End-diastole was defined as frame 2; frame 1 was not used as counts may be lost due to the formatting process. Two frames at end-systole were summed and smoothed to give the stystolic image used for processing. The process was repeated for two end-diastolic frames. Although true end-systole (minimum ventricular volume) is usually only 30–40 ms in duration, rather than the 70 ms represented by two frames (at a heart rate of 60), it was found that the difference in the edge position varied very little if two frames were taken, and it was felt that this was outweighed by the statistical advantage achieved by summing adjacent frames.

The first two methods employed an isocount edge, placed around the left ventricle in both systole and diastole. To determine the height of the isocount, a band 2 cm wide was placed perpendicular to the long axis of the ventricle over the area of maximum counts. From this band a profile of the counts was generated and the maximum of its first derivative used to define the height for the isocount contour, thus avoiding subjective variations in the isocount height. This is similar to the method used by Hecht *et al.* (1978).

Motion was then assessed for each segment for each patient by viewing the systolic and diastolic edges, displayed sequentially (moving edge) or superimposed (static edge). The thid method used a commercially available programme (MUGE) which employed a two-dimensional second derivative to select the ventricular edge. The two summed frames were smoothed ten times before determining the edge; this method is very sensitive to noise and the outline was difficult to interpret if fewer smooths were used. Systolic and diastolic edges were superimposed and the degree of motion assessed as before. To assess inter-observer variability of the radionuclide methods, a second operator repeated the assessment of wall motion for all four methods.

Scoring system

In order to determine the measure of agreement between the methods a "difference score" was calculated in which the score for equilibrium radionuclide angiography was subtracted from the score for contrast angiography (as this is the standard) for each of the four methods of radionuclide analysis. The "difference score" limits are +3 or −3 depending on the degree of underestimation or overestimation of motion assessed by the radionuclide methods with respect to contrast angiography. The possible range of "difference scores" is given in Table I.

Five equal segments were chosen by visual subdivision of the circumference of the ventricle. If more than one degree of motion was present in a given segment, an average score was given.

RESULTS

The results were assessed independently for equilibrium radionuclide angiography and contrast angiography, and a score given for the motion of each of the five segments of the left ventricle, for the two techniques, based on the four point scale described earlier.

The results for each segment for the 36 patients are presented in Table II for the FINE display versus contrast angiography. The results for the other methods of analysis show a similar distribution.

TABLE I

POSSIBLE DIFFERENCE SCORES FROM VARIOUS ASSESSMENTS OF WALL MOTION (CA—ERA). 0 = EXACT AGREEMENT

		Cineangiography			
		Good (0)	Hypokinesis (1)	Akinesis (2)	Dyskinesis (3)
Equilibrium radionuclide angiography	Good (0)	*0*	1	2	3
	Hypokinesis (1)	−1	*0*	1	2
	Akinesis (2)	−2	−1	*0*	1
	Dyskinesis (3)	−3	−2	−1	*0*

TABLE II

RESULTS OF ASSESSMENT OF WALL MOTION FOR CINEANGIOGRAPHY AND FINE

Patient No.	Left ventricular segments										
	Apex		Prox. ant		Dist. ant		Prox. dia		Dist. dia		
	CA	FINE	CA	FINE	CA	FINE	CA	FINE	CA	FINE	
1	0	0	0	0	0	0	1	0	1	0	A
2	2	1	0	0	1	1	2	0	2	1	A
3	0	0	0	0	0	0	0	1	0	0	AS
4	2	1	1	1	1	1	2	2	2	1	AR/LVF
5	0	0	0	0	0	0	0	0	0	0	A
6	2	2	2	0	2	2	2	1	2	2	AR
7	3	2	1	1	2	1	1	0	3	2	A/AR
8	0	0	0	1	0	0	0	1	0	0	A
9	0	0	0	0	0	0	0	0	0	0	AS
10	1	0	0	0	1	0	1	2	1	0	MR/LVF
11	2	2	1	0	2	1	0	1	2	0	A/AR/LVF
12	2	2	0	0	1	1	1	1	2	1	A
13	2	2	1	0	2	1	0	0	1	0	AS
14	2	1	1	0	2	1	1	1	2	1	AS/AR
15	3	2	0	0	2	1	1	0	2	2	A
16	3	2	1	0	2	2	0	0	1	0	A
17	0	0	0	0	0	0	0	0	0	0	AR
18	0	0	0	0	0	0	0	0	0	0	AS
19	2	2	0	1	2	1	2	2	1	1	A
20	2	2	0	0	2	2	0	0	2	2	A/AS
21	2	2	1	1	2	2	0	0	2	0	A
22	3	3	0	1	2	2	0	0	3	3	A/AR
23	2	2	0	1	2	1	1	0	2	1	A
24	1	1	0	0	2	2	0	0	1	1	A
25	0	0	0	0	0	0	0	0	0	0	AS
26	0	0	0	0	0	0	0	0	0	0	A
27	0	0	0	0	0	0	0	1	0	0	A
28	0	2	0	0	0	0	1	0	1	0	A/MR
29	2	2	0	0	1	1	1	0	2	2	AS/AR
30	1	0	0	0	1	0	0	0	2	1	MS
31	1	2	1	0	2	2	1	1	2	1	A
32	3	3	1	1	2	2	1	1	1	1	A/AR
33	3	3	0	0	1	2	0	0	1	1	A
34	0	0	0	0	0	0	0	0	0	0	A
35	1	2	1	2	1	2	1	2	2	2	A/AR
36	0	0	0	0	0	0	0	0	0	0	MR

A = Angina; AS = Aortic stenosis; AR = Aortic regurgitation; MS = Mitral stenosis; MR = Mitral regurgitation; LVF = Left ventricular failure.

Inter-observer variability for radionuclide angiography

The same degree of motion was chosen by the two operators using radionuclide methods in 530 out of 720 segments (36 patients ×5 segments ×4 methods of analysis). In no case was there a difference of more than one degree of motion. No difference was seen between the four methods.

Segmental results

The histograms (Figs. 1–4) show the difference scores obtained for each method, segment by segment.

Exact agreement

One method, FINE, showed exact agreement in 70% of cases in anterior and apical segments, 59% in the diaphragmatic segment (average for all segments 67%). The three edge methods produced similar results, averaging 50% (52–47) in anterior and apical segments, 45% (47–43) in the diaphragmatic segments (average for all segments 47%). Table III shows the segmental degree of agreement for the method FINE, and Table IV the overall agreement for each method. In 180 segments, FINE differed from contrast angiography in two points in five (3%).

Table III shows that equilibrium radionuclide angiography with the FINE display tends to underestimate wall motion. This may partly be due to overlapping of the left ventricle by the right ventricle since Fig. 1 shows the underestimation to be greatest in the diaphragmatic segments.

Figure 5 shows the agreement between contrast angiography and equilibrium radionuclide angiography for the five segments of the left ventricle.

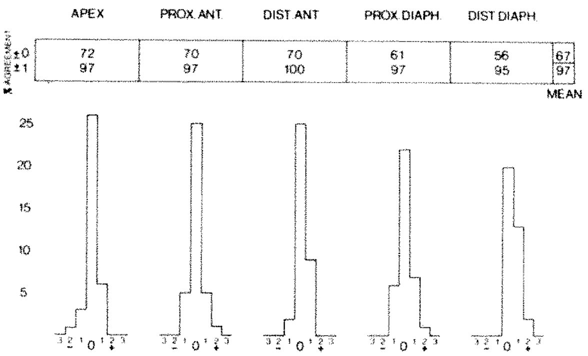

FINE Difference Scores

FIG. 1.

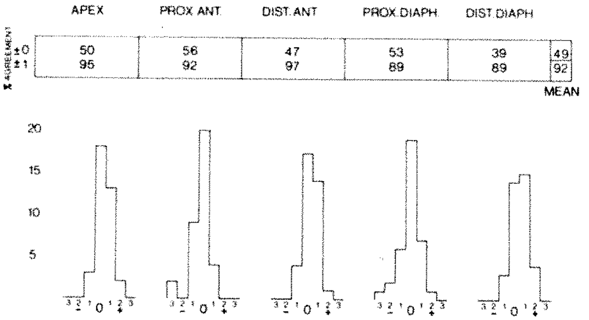

STATIC EDGE Difference Scores

FIG. 2.

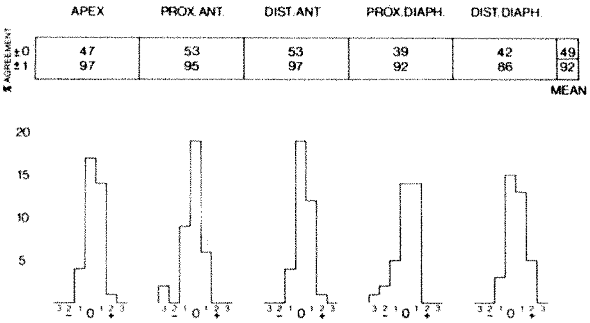

MOVING EDGE Difference Scores

FIG. 3.

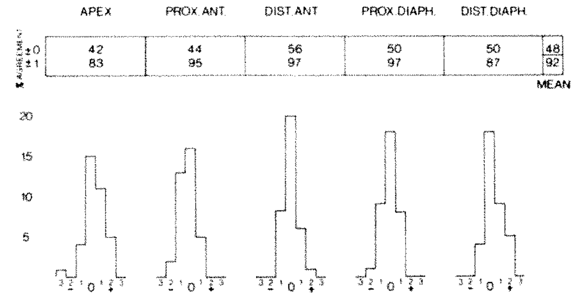
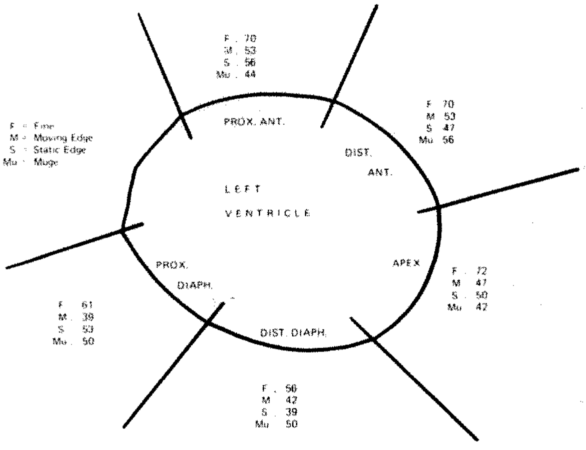

MUGE Difference Scores

FIG. 4.



% Exact Agreement between C.A. & E.R.A. on a 4 point scale

FIG. 5.

TABLE III

Degree of agreement of segmental wall motion between contrast angiography and equilibrium radionuclide angiography for the FINE display

		Equilibrium radionuclide angiography (FINE)			
		Normal	Hypokinetic	Akinetic	Dyskinetic
Contrast Angiography	Normal	73	8	1	—
	Hypokinetic	18	19	7	—
	Akinetic	6	16	24	—
	Dyskinetic	—	—	4	4

TABLE IV

Percent agreement of the four methods with contrast angiography

	±0	±1	±2	±3
FINE	67	30	3	—
Moving edge	49	43	16	2
Static edge	49	43	16	21
MUGE	48	44	7	1

Discussion

Several authors (Zaret *et al.*, 1971; Burow *et al.*, 1977) have used equilibrium radionuclide angiography to assess left ventricular wall motion. It has been stated (Pierson *et al.*, 1977; Hecht *et al.*, 1978) that only the two anterior and apical segments can be seen in equilibrium studies, since in the 30° RAO projection the right ventricle overlies the diaphragmatic segment of the left ventricle. There has not, however, been a segmental evaluation of equilibrium studies in this view to assess this claim.

Our results confirm that assessment of left ventricular wall motion using edge detection methods is less accurate in the diaphragmatic than in the apical and anterior segments. In our study, the correlation with contrast angiography is greater than has been supposed; this could, however, reflect a tendency for patients with poor left ventricular segments to have abnormal right ventricular segments.

Contrast angiography derives much of its information from relative rates of motion, which cannot be shown by a static image. It has been suggested (Borer *et al.*, 1977; Strauss and Pitt, 1978), therefore, that more information would be provided by a method showing motion. In this study the cine display gave a definite impression of left ventricular motion "behind" the right ventricle, with 97% agreement for the proximal diaphragmatic segment and 95% agreement for the distal diaphragmatic segment to within one degree of motion. This close correlation supports the subjective impression of left ventricular wall motion. Tomographic equilibrium imaging should be able to clarify this contention. If a cine display is used for analysis, the diaphragmatic segments would seem not to merit the title "hidden" (Pierson *et al.*, 1977).

The second and third methods using an edge display (moving and static edge) showed more than 86% close agreement (± one degree) in all segments. The sequential end systolic–end diastolic display (moving edge) did not offer increased accuracy over the static display, since the frames used for display were identical for the two methods. Strauss and Pitt (1978) and Garcia *et al.* (1977) have used the first pass of the radioactive bolus to determine the positions of the valve planes and the two diaphragmatic segments in addition to the equilibrium study, in order to give information about the complete left ventricle. This would appear to be unnecessary if the cine display method of analysis is used, although it may still be of benefit where edge detection methods are employed for the assessment of wall motion.

Hecht *et al.* (1978) studied 21 patients, comparing cine angiography with first pass radionuclide angiography. The proportion of segments with normal motion to those with hypokinesia was similar to the present study. Exact agreement was reached in 70 out of 105 segments (72%) with agreement to within one degree in 101 segments (98%). This is similar to our results using the cine display (67% exact agreement, 97% to within one degree), and suggests that equilibrium radionuclide angiography can match the accuracy of first pass techniques in the RAO projection. First pass studies for the detection of wall motion show similar accuracy in all segments, and this is an important advantage over equilibrium imaging where edge detection methods are used.

From this study it can be seen that the cine display provides information on all five segments of the left ventricle in the RAO projection with an accuracy equal to that of the first pass studies. With equilibrium imaging already established for viewing the septum and posterior segments in the LAO projection, we conclude that equilibrium radionuclide angiography with a cine display of analysis is the method of choice for non-invasive investigation of suspected regional wall motion abnormalities.

Acknowledgments

We wish to thank Dr. A. Johnson for allowing us to study the patients under his care, and Mrs. Sheila Foulkes for typing the manuscript. The project was supported by a research fellow funded by Boehringer Ingelheim (UK) Ltd.

REFERENCES

Borer, J. S., Bacharach, S. L., Green, M. V., Kent, K. M., Epstein, S. E. and Johnston, G. S., 1977. Real time radionuclide cineangiography in the non-invasive evaluation of global and regional left ventricular function at rest and during exercise in patients with coronary artery disease. *New England Journal of Medicine, 296*, 839–844.

Burow, R. D., Strauss, H. W., Singleton, R., Pond, M., Rehn, T., Bailey, I. K., Griffith, L. C., Nickoloff, E. and Pitt, B., 1977. Analysis of left ventricular function from multiple-gated acquisition cardiac blood pool imaging: comparison to contrast angiography. *Circulation, 56*, 1024–1028.

Garcia, E., Sardi, E., Hammer, S., Koorji, A., Mallon, S. and Gottlieb, S., 1977. A method for isolating the left ventricle in the right anterior oblique projection from equilibrium gated blood pool radionuclide imaging. *Circulation Abstracts, 55 and 56*, 193.

Hecht, H. S., Mirell, S. G., Rolett, E. L. and Blahd, W. H., 1978. Left ventricular ejection fraction and segmental wall motion by peripheral first-pass radionuclide angiography. *Journal of Nuclear Medicine, 19*, 17–23.

Pierson, R. N., Alam, S. and Kemp, H. G., 1977. Radiocardiology in clinical cardiology. *Seminar in Nuclear Medicine*, 7, 85–100.

Strauss, H. W. and Pitt, B., 1978. Evaluation of cardiac function and structure with radioactive tracer techniques. *Circulation, 57*, 645–654.

Zaret, B. L., Strauss, H. W., Hurley, P. J., Natarajan, T. K. and Pitt, B., 1971. A non-invasive scintiphotographic method for detecting regional ventricular dysfunction in man. *New England Journal of Medicine, 284*, 1165–1170.

Book reviews

Cardiac Nuclear Medicine. Edited By B. L. Holman, A. L. Abrams and E. Zeitler, pp. 88 ill. 1979 (Springer-Verlag, Berlin/Heidelberg/New York), DM.35/$19.60.
ISBN 3-540-09803-8.

The considerable literature that has accumulated during recent years in the field of radioisotope cardiology has tended to leave non-experts unclear as to the place of the different radionuclide procedures for solving particular clinical problems. Although this slim volume (published in 1979) does not precisely answer this question it does provide a very good summary of procedures which are available for both routine and research investigation.

The book is introduced by Dr. Holman with a clear statement of the various technical possibilities, and this is followed by specialist chapters on first-pass and equilibrium gated methods, myocardial imaging with infarct-avid tracers and thallium, rest/exercise imaging, inert gas wash-out techniques, and emission tomography. The multi-author approach inevitably leads to some unevenness of presentation, and at times too great an emphasis is placed on personal experience. This is notable in the chapter on equilibrium gated studies where the prominence of Fourier analysis and parametric images tends to obscure the importance of these procedures for routine measurement of ejection fraction and regional wall motion. The chapter on myocardial imaging with infarct avid tracers is a refreshingly honest evaluation of the limitations of this technique. Those dealing with exercise thallium studies and the measurement of absolute coronary blood flow by inert gas washout analysis are clearly structured and written. That on thallium quantification shows that an improvement in sensitivity and specificity can be gained over analogue imaging, but that scrupulous attention to analytical technique is necessary if results are to be reproducible. The final chapter describes clearly the present status of emission tomography for cardiac investigations.

The fact that this publication is already a year old means that there are certain omissions—notably of recent developments in alternative methods to exercise for the investigation of patients with transient myocardial ischaemia. There is also rather limited discussion of the errors of measurement (statistical, background, etc.) which may limit the accuracy of some procedures. In general, the editors have succeeded in their aim to give the cardiac (and nuclear) physicians an inexpensive and up-to-date view from both sides of the Atlantic of what can be offered in this subject. Those intending to start, or already providing, a radionuclide cardiac service will find this book full of useful information.

D. M. Ackery.

ABC Radiodiagnostic. 3. Radiologie vasculaire. By J. Chermet. 1979. pp. viii + 157. (Masson, Paris).
ISBN 2-225-64372-5

This is a small-format modestly-priced volume about techniques and indications for vascular radiology. No radiological illustrations are provided, but a fair number of didactic schemes should compensate for this shortcoming.

The author has successfully brought together up-to-date essential information on vascular radiological techniques with an accent on the practical aspects and rules involved. If necessary, alternative less-used methods are relevantly discussed and the technical description of each method of examination is followed by a critical evaluation of current clinical indications.

One of the main qualities of this book is the fact that it is written from a broad clinical experience and background and that it is very complete despite its small size. As a practical guide it will be useful for students doing their training in vascular radiology. For differential diagnosis it needs, of course to be complemented by a manual with fully illustrated descriptions of the individual pathological entities.

A. Baert.

1981, *British Journal of Radiology*, *54*, 302–306

Comparison of intravenous radionuclide cholescintigraphy and endoscopic retrograde cholangiography in the diagnosis of intrahepatic gall-stones

By Miau-Ju Huang, M.D., Yun-Fan Liaw, M.D.*, and Cheng-Shyong Wu, M.D.*

Departments of Nuclear Medicine and *Internal Medicine, Chang Gung Memorial Hospital, Taipei, Taiwan, Republic of China

(*Received January 1980 and in revised form June 1980*)

Abstract

Intravenous radionuclide cholescintigraphy using ^{99}Tc^{m}-pyridoxylideneglutamate (Tc-99m-PG) has been compared with endoscopic retrograde cholangiography (ERC) as a test for the pre-operative detection of intrahepatic gall-stones.

Sixty-three patients, 42 of whom were clinically jaundiced, were studied and 27 of these were subsequently shown to have intrahepatic gall-stones. Cholescintigraphy correctly predicted stones in all but five of these patients (false negative 19%), while ERC failed to show intrahepatic stones in seven patients (false negative 26%). In the 36 patients found to have no intrahepatic stones, cholescintigraphy was incorrect in six patients (false positive 17%) and ERC incorrect in two (false positive 6%).

Cholescintigraphy is at least as successful as ERC in predicting intrahepatic gall-stones and is cheaper and less invasive. In populations where intrahepatic gall-stones are common, it is likely to prove valuable as a pre-operative screening test.

Intrahepatic gall-stones are relatively common in orientals but are rarely encountered in the Western World (Maki *et al.*, 1964; Balasegaram, 1972; Maki *et al.*, 1972; Wen and Lee, 1972). In a recent report from Taiwan, 39 (17.6%) of 221 biliary operations had intrahepatic stones (Jan *et al.*, 1978). Unlike cholelithiasis and choledocholithiasis, intrahepatic stones are a difficult problem to biliary surgeons because of the high incidence of retained stones (Chen *et al.*, 1979).

Although accurate preoperative demonstration of intrahepatic stones can be made by percutaneous transhepatic cholangiography (PTC) (Maki *et al.*, 1964; Balasegaram, 1972; Maki *et al.*, 1972; Wen and Lee, 1972), and/or endoscopic retrograde cholangiography (ERC) (Wang and Sung, 1977), both PTC and ERC are uncomfortable and intolerable to certain patients (Elias *et al.*, 1976). An alternative accurate, simple, safe and non-invasive diagnostic test would allow clinicians to make a diagnosis of intrahepatic stone more easily before surgery.

Since the introduction of ^{99}Tc^{m}-pyridoxylideneglutamate (Tc-99m-PG) cholescintigraphy (Ronai *et al.*, 1975), intravenous radionuclide cholescintigraphy (IVRC) has proved to be a useful diagnostic tool for biliary diseases (Stadalnik *et al.*, 1976, 1978; Matolo *et al.*, 1976; Ronai, 1977; Pauwels *et al.*, 1978; Jenner *et al.*, 1978a, 1978b; Craig *et al.*, 1978). Its diagnostic value in gall-bladder diseases and intrahepatic stones was also confirmed in Taiwan (Yeh *et al.*, 1977, 1980; Wang *et al.*, 1978; Huang *et al.*, 1979). We have therefore compared IVRC and ERC as pre-operative tests for intrahepatic stones.

Patients and Methods

1. *Patients*

During a nine month period, 30 normal controls and 141 patients with suspected biliary disease were seen, 96 of whom received biliary surgery. In 63 of these, preoperative IVRC and ERC were successfully performed. In a further 15 patients ERC was attempted, but failed.

The serum bilirubin of these 63 patients ranged from 0.8 to 10 mg% (normal < 1 mg%) with a mean value 4.8 mg%. Ten of them had a normal bilirubin level and 21 (33.3%) had a bilirubin level $\leqslant 2$ mg%.

The intrahepatic ducts were checked routinely whenever the common bile duct was explored during operation. Liver biopsy was done in each case. T-tube cholangiography and choledochoscopy were also performed routinely four weeks after operation. Twenty-seven of the patients proved to have intrahepatic stones. The others included 21 with common bile duct stones, nine with gall-bladder stones, three with a periampullary tumour, two with cholangiocarcinoma, and one with hepatoma.

2. *Methods*

ERC was performed using Olympus JFB2 or JFB3. The diagnosis of intrahepatic stones was made when one or more stones were demonstrated in the ducts above the common hepatic duct (Fig. 1).

Tc-99m-PG was prepared by the method of Baker *et al.* (1975), and 4–6 mCi of Tc-99m-PG was injected intravenously after overnight fasting. Serial cholescintigrams were taken at 5, 15, 30, 60, 120,

---

For reprints contact Miau-Ju Huang, M.D., Dept. of Nuclear Medicine, Chang Gung Memorial Hospital, Taipei, Taiwan 105, Republic of China.

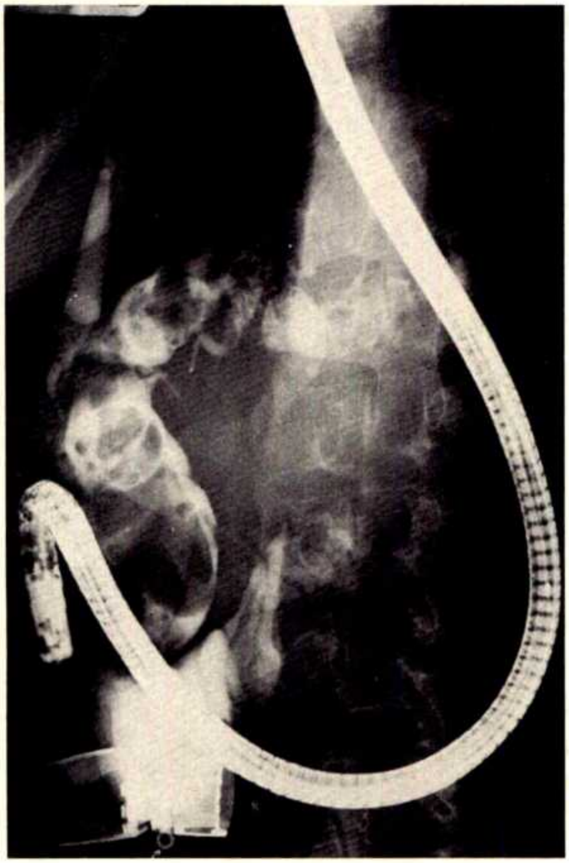


FIG. 1.

ERC of a patient showing multiple radiolucent shadows in left intrahepatic duct and also common bile duct.

240, 360 min and 24 hrs after injection. The diagnosis of intrahepatic stones was made when IVRC showed: 1. intrahepatic cold area in the initial image, 2. prolonged pooling of radioactivity at the corresponding area in the late images ($\geqslant$4 hrs) (Fig. 2). Partial stasis of biliary excretion was not considered as an essential criterion (Fig. 3), because of its high false negative and false positive rates (Yeh *et al.*, 1977, 1980). All of the diagnoses were made independently before ERC and surgery.

The accuracy of IVRC and ERC were assessed according to operative findings.

RESULT

TABLE I

THE DIAGNOSTIC ABILITY OF Tc-99M-PG CHOLESCINTIGRAPHY AND ERC IN INTRAHEPATIC STONE

	Operative findings Intrahepatic stone	
Tests	Present (n=27)	Absent (n=36)
IVRC Correct	22	30
Incorrect	5 (18.5%)	6 (16.7%)
ERC Correct	20	34
Incorrect	7 (25.9%)	2 (5.6%)

TABLE II

COMPARISON OF Tc-99M-PG CHOLESCINTIGRAPHY AND ERC IN THE DIAGNOSIS OF INTRAHEPATIC STONE

	IVRC (n=63)	ERC (n=63)
Sensitivity	81.5%	74.1%
Specificity	83.3%	94.4%
Predictive value	78.6%	90.9%
Efficiency	82.5%	85.7%

Of 63 patients who had both IVRC and ERC before operations, 27 were proved to have intrahepatic stones. The correct diagnosis was made by IVRC in 22 (81.5%) and by ERC in 20 (74.1%). Slightly more false positive reports were obtained by IVRC (16.7%) than by ERC (5.6%). (Table I). The sensitivity, specificity, predictive value and efficiency of these two tests are shown in Table II.

A further 15 patients had ERC attempted but failed and the local success rate of ERC would need to be taken into account when deciding which test to use for screening purposes. Complications in the ERC series included six (9.5%) having transient abdominal pain requiring analgesics, five (7.9%) had transient hyperamylasaemia, seven (11.1%) developed spiking fever and one (1.6%) sepsis.

No significant discomfort, side effects or failure was encountered in the IVRC series.

The cost of ERC is two to three times higher than that of IVRC in this hospital.

DISCUSSION

An ideal diagnostic tool should be sensitive, specific, simple and safe. Oral cholecystography (OC) and intravenous cholangiography (IVC) almost match these criteria in the diagnosis of biliary diseases (Rosenbaum, 1974; Sung *et al.*, 1963). Unfortunately, these examinations exclude the study of intrahepatic ducts, and are also limited by extrabiliary factors, such as impaired liver function and hyperbilirubinaemia greater than 3 mg% (Sung *et al.*, 1963; Fischer, 1966). They play no role in the diagnosis of intrahepatic stones because almost all of these patients are jaundiced or have impaired liver function during the acute attack (Wen and Lee, 1972). PTC and ERC demonstrate intrahepatic ducts best (Maki *et al.*, 1964, 1972; Balasegaram, 1972; Wen and Lee, 1972; Wang and Sung, 1977) in the patient with jaundice and poor liver function. PTC is an invasive procedure but is not always successfully performed and is sometimes intolerable to certain patients (Elias *et al.*, 1976). ERC is probably safer and less invasive than PTC (Wang and Sung, 1977), but is technically difficult, time-consuming, uncomfortable for the patients, and as yet available in relatively few institutions (Ronai, 1977). ERC and PTC are both useful for definite anatomical diagnosis but not ideal for routine screening. If there were a diagnostic tool as sensitive and specific as PTC and ERC in the diagnosis of intrahepatic stones, and as simple and safe as OC and IVC, it would become an ideal diagnostic tool for this condition.

Intravenous radionuclide cholescintigraphy (IVRC) using Tc-99m-PG provides a simple and

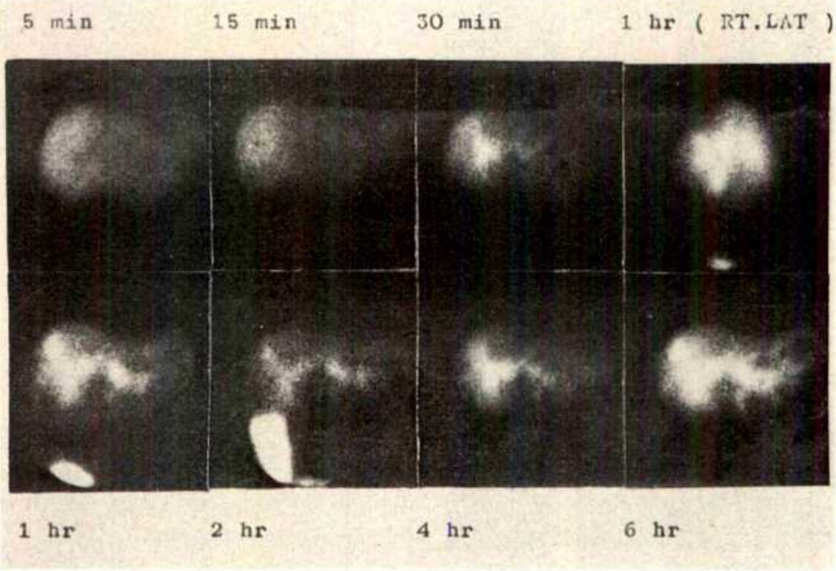


Fig. 2.

Sequential Tc-99m-PG cholescintigrams of the same patient shown in Fig. 1. Note cold areas suggestive of biliary dilatation in cholescintigram at 5 min, prolonged pooling of radioactivity in both lobes as shown in cholescintigrams at 4 and 6 h, and also delayed appearance of radioactivity in the bowel later than 1 h.

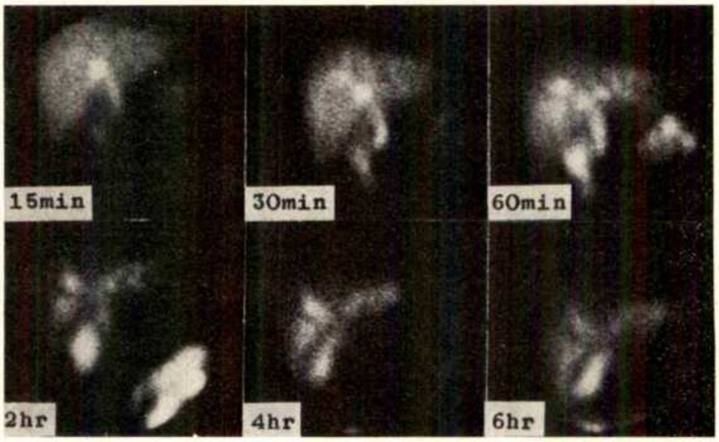


Fig. 3.

Sequential Tc-99m-PG cholescintigrams in another case show a cold area at 5 min, prolonged pooling up to 4 and 6 hrs, but appearance of the tracer in bowel within 30 min.

safe functional study of the whole biliary system, and its diagnostic value has been widely confirmed in biliary disease (Ronai *et al.*, 1975; Stadalnik *et al.*, 1976, 1978; Matolo *et al.*, 1976; Ronai, 1977; Pauwels *et al.*, 1978; Jenner *et al.*, 1978a, 1978b; Craig *et al.*, 1978; Huang *et al.*, 1979). Yeh *et al.* (1977) first mentioned the diagnostic criteria of Tc-99m-PG cholescintigraphy and its diagnostic value in intrahepatic stones. Wang *et al.* (1978) also suggested that Tc-99m-PG cholescintigraphy is an effective, non-invasive, simple procedure in the diagnosis of intrahepatic stones using similar criteria. Their observations were based on a limited number of cases and the effectiveness was not compared with other diagnostic modalities.

Our results in Table II show that Tc-99m-PG cholescintigraphy is a sensitive and effective tool for the diagnosis of intrahepatic stone. False positives were obtained only in patients with common bile duct stones causing the subsequent dilatation of intrahepatic ducts.

In comparison with ERC, IVRC is more sensitive in the diagnosis of intrahepatic stones possibly because small "muddy" stones impacted at the bifurcation of intrahepatic ducts may be missed by ERC (as well as by PTC) (Yeh *et al.*, 1980). On the other hand, ERC was successfully performed in only 80.8% in our hands and this seems comparable with the success rate in many other centres. If this factor is considered, the detection rate of IVRC would be even greater than that of ERC.

ERC visualizes the biliary system in a retrograde fashion so that details of intrahepatic ducts occasionally cannot be demonstrated if a stone is impacted at the orifice of a duct. For example, Fig. 1 demonstrated left intrahepatic stones clearly but there was no evidence of stones visualized in the ducts of the right lobe. In this instance, IVRC can provide more information because IVRC visualizes the entire biliary tree by the excretion of the radionuclide by hepatocytes. IVRC of the same patient (Fig. 2) showed intrahepatic stasis in the right lobe as well as the left lobe. Subsequent operation proved there were stones in both lobes.

This study clearly shows that IVRC is not only simple, safe, non-invasive and less expensive, but also at least as successful as ERC in predicting intrahepatic stone. IVRC cannot provide the same anatomical information as ERC or PTC, and careful cholangiography will still be needed prior to surgery if intrahepatic stones are implicated by IVRC. However, in populations where intrahepatic stones are common, IVRC is likely to prove valuable as a preoperative screening test.

ACKNOWLEDGMENT

The authors are indebted to Prof. S. H. Yeh of Taiwan Veterans General Hospital for his invaluable instruction in this work, and the technical assistance of Miss S. W. Yeh, Miss S. H. Lin and Mr. K. R. Chang.

This work was supported in part by Chang Gung Research Grant MRP-027.

REFERENCES

Baker, R. J., Bellen, J. C. and Ronai, P. M., 1975. Tc-99m-PG: a new hepatobiliary radiopharmaceutical: experimental aspects. *Journal of Nuclear Medicine, 16*, 720–727.

Balasegaram, M., 1972. Hepatic calculi. *Annals of Surgery, 175*, 149–154.

Chen, M. F., Chou, F. F. and Wang, C. S., 1979. Removal of retained biliary stone by choledochofiberscope. *Journal of Formosan Medical Association, 78*, 761–766.

Craig, J. O. M. C., Hinton, J., Murphy, F. and Glazer, G., 1978. Hepatobiliary scanning in jaundice. *Lancet, ii*, 632.

Elias, E., Hamlyn, A. N., Jain, S., Long, R. G., Summerfield, J. A., Dick, R. and Sherlock, S., 1976. Randomized trial of percutaneous transhepatic cholangiography with the chiba needle versus endoscopic retrograde cholangiography for bile duct visualization in jaundice. *Gastroenterology, 71*, 439–443.

Fischer, H. W., 1966. Physiologic and pharmacologic aspects of cholangiography. *Radiologic Clinics of North America, 4*, 625–632.

Huang, M. J., Yeh, H. R. and Liaw, Y. F., 1979. Diagnostic value of Tc-99m-PG cholescintigraphy in gall bladder diseases. *Journal of Formosan Medical Association, 78*, 252–257.

Jan, Y. Y., Chen, M. F., Chou, F. F., Wang, C. S., Liaw, Y. F. and Chen, L., 1978. Histopathologic changes of the liver in diseases of biliary calculi. *Chang Gung Medical Journal, 3*, 3–6.

Jenner, R. E., Howard, E. R., Clark, M. B. and Barrett, J. J., 1978a. Hepatobiliary imaging: a comparison of ^{99}Tc^{m}-dihydrothioctic acid and ^{99}Tc^{m}-pyridoxylideneglutamate in the nonjaundiced patient. *British Journal of Radiology, 51*, 858–861.

1978b. Hepatobiliary imaging: the use of ^{99}Tc^{m}-pyridoxylideneglutamate scanning in jaundiced adults and infants. *British Journal of Radiology, 51*, 862–866.

Maki, T., Scato, T. and Matsushiro, T., 1972. A reappraisal of surgical treatment for intrahepatic gall stones. *Annals of Surgery, 175*, 155–165.

Maki, T., Sato, T., Yamaguchi, I. and Sato, T., 1964. Treatment of intrahepatic gall stones. *Archives of Surgery, 88*, 124–134.

Matolo, N. M., Stadalnik, R. C. and Wolfman, E. R., 1976. Clinical evaluation of Tc-99m-PG for hepatobiliary scanning. *American Journal of Surgery, 132*, 716–719.

Pauwels, S., Steels, M., Piret, L. and Beckers, C., 1978. Clinical evaluation of Tc-99m-diethyl-IDA in hepatobiliary disorders. *Journal of Nuclear Medicine, 19*, 783–788.

Ronai, P. M., 1977. Hepatobiliary radiopharmaceuticals: Defining their clinical role will be a galling experience. *Journal of Nuclear Medicine, 18*, 488–490.

Ronai, P. M., Baker, R. J., Bellen, J. C., Collins, P. J., Anderson, P. J. and Lander, H., 1975. Tc-99m-PG: a new hepatobiliary radiopharmaceutical: II. Clinical aspect. *Journal of Nuclear Medicine, 16*, 728–737.

Rosenbaum, H. D., 1974. An evaluation of oral cholecystography. *Journal of the American Medical Association, 229*, 76–79.

Stadalnik, R. C. and Matolo, N. M., 1978. Value of Tc-99m-PG scintigraphy in the evaluation of the jaundiced patient. *International Journal of Nuclear Medicine and Biology, 5*, 176–182.

Stadalnik, R. C., Matolo, N. M., Jansholt, A. L., Krohn, K. A., DeNardo, G. L. and Wolfman, E. F., 1976. Tc-99m-PG cholescintigraphy. *Radiology, 121*, 657–661.

Sung, J. L., Chiu, W. S. and Chen, P. H., 1963. Intravenous cholangiography. *Journal of Formosan Medical Association, 62*, 599–610.

Wang, C. S., Chen, P. H. and Siauw, C. P., 1978. Diagnosis of intrahepatic stone by Tc-99m-PG cholescintigram. *Journal of Formosan Medical Association, 77*, 525–532.

Wang, T. H. and Sung, J. L., 1977. Endoscopic retrograde cholangiopancreatography. *Journal of Formosan Medical Association, 76*, 91–106.

Wen, C. C. and Lee, H. C., 1972. Intrahepatic stones: a clinical study. *Annals of Surgery, 175*, 166–177.

Yeh, S. H., Liu, O. K. and Huang, M. J., 1977. Technetium-99m-pyridoxylideneglutamate (Tc-99m-PG) sequential scintiphotography in the detection of intrahepatic stones (*Abstract*). *Journal of Nuclear Medicine, 18*, 635.

1980. Sequential scintiphotography with technetium-99m-pyridoxylideneglutamate in the detection of intrahepatic lithiasis: Concise communication. *Journal of Nuclear Medicine, 21*, 17–21.

Book reviews

Nuclear Medicine Physics, Instrumentation and Agents. Edited by F. D. Rollo, pp. xiv+698, ill., 1977 (C. V. Mosby, US.A.; Henry Kimpton, London), £41·60.

The stated purpose of this substantial text book is to provide a complete and up-to-date account dealing exclusively with the physics and instrumentation of nuclear medicine. Aiming to be up-to-date is of course aiming at a moving target and inevitably some of the fashionable preoccupations of nuclear medicine specialists at the time of printing, such as for example nuclear cardiology, have been missed at the time of writing. In addition, as is so often the case, the tacit assumption has been made that nuclear medicine is synonymous with radionuclide imaging. The physics of *in-vitro* techniques, tracer studies, dosimetry and the biological effects of radiation have largely been excluded. However the topics which do find a place are sometimes dealt with to a greater depth than in other contemporary texts and provide the reader with a rare opportunity to select information to the level required.

The chapters on atomic and nuclear physics include much detail of marginal relevance such as models of the nucleus and the Mössbauer effect, which are more appropriate to the early stages of a degree course in physics. The chapters on electronics are also remarkable for their extent but they contain an exceptionally lucid explanation of pulse shaping in scintillation counters which is of great practical importance in the selection of the optimum operating conditions for equipment.

The Anger camera and rectilinear scanner are described with useful reference to the techniques employed in particular models. Strangely, quality assurance in imaging is discussed before the factors affecting image formation, but taken together these sections provide a comprehensive guide to good technique. Methods recommended for the evaluation of imaging devices inevitably reflect the techniques preferred by the authors. The concept of contrast efficiency, for example, is not well known and its use to describe how well an imaging device will perform in a clinical situation, while illuminating the issues involved, is of debatable validity.

Other topics such as computers, radiation safety, internal dosimetry and radiopharmaceuticals are all covered to some extent, but as in many multi-author texts the balance is not always well judged. There is obvious duplication when for example the operation of the gamma camera is described in different chapters and the same photographs of a particular phantom are given in different figures. The text and illustrations are generally clear and free of errors although if the current curve for an ionisation chamber had been drawn correctly it would have been more difficult to describe its operation without a mention of the recombination of ions.

It is not obvious for whom this text was designed. Physicists, technologists and clinicians would all be likely to learn from parts of it but the whole would be unlikely to be essential reading. It can be strongly recommended for the departmental shelves.

M. F. Cottrall.

Quality Assurance Measurements in Diagnostic Radiology. HPA Conference Report Series 29. 1979. pp. 72. (Hospital Physicists' Association, London). £4·00.
ISBN 0–904181–14–6

This Report of the HPA Conference held in October 1978, published in 1979, indicates progress since the previous meeting in 1976, and forms a useful summary of the state of the art. It includes sections on radiographic control and reproducibility, performance of image intensifier systems, and logistics for assurance tests.

The programme was well balanced between hospital physicists, manufacturers, radiologists and radiographers. It included detailed and critical descriptions of some test systems presently in use, with comments related to national and international standards specifications. Results of measurements in the field provided fertile grounds for the discussions reported in this book. Various sections include contributions from representatives of the Department of Health and Social Security and an American physicist well known in this field, and help to put the philosophy of quality control into perspective.

This paperbacked text is liberally provided with diagrams which makes for easy reading and quick reference. It is an essential for all those concerned with X-ray quality control.

B. E. Keane.

1981, *British Journal of Radiology*, *54*, 307–311 APRIL 1981

Ultrasound in hepatoma—can specific diagnosis be made?

By P. A. Dubbins, M.B., B.S., F.R.C.R.*, D. O'Riordan, M.B., B.Ch., F.R.C.R. and
W. M. Melia, M.B., M.R.C.P., M.R.C.P.I.

The Department of Diagnostic Radiology and the Liver Research Unit, King's College Hospital,
Denmark Hill, London SE5

ABSTRACT

The ultrasound appearances of primary hepatocellular carcinoma in 32 patients are described. Attempts to correlate the appearances with serological, histological, and arteriographic findings revealed no consistent pattern. There appears to be no great difference in the range of ultrasound appearances in primary hepatocellular carcinoma when compared with that reported for metastatic disease. The findings suggest that in patients with cirrhosis, ultrasound is a sensitive method for the detection and accurate location of hepatocellular carcinoma, but that in these patients the echo pattern provides little help in the differentiation of primary from secondary carcinoma. Our study has revealed four different echo patterns in patients with hepatocellular carcinoma: echofree (47%), echogenic (23%), mixed (17%) and diffuse infiltration 13%).

Primary hepatocellular carcinoma is not a common tumour in Great Britain. In 1977 there were only 489 recorded deaths attributable to this tumour in the General Registry for England and Wales (Office of Population Censuses and Surveys, 1977). Primary hepatocellular carcinoma is on the increase, possibly due to increased life expectancy in cirrohrics as a result of improved supportive therapy (Peters *et al.*, 1977).

In other parts of the world, particularly Southern Africa and the Far East, the tumour is considerably more common (Anthony, 1973). This variability of incidence is thought to be due to environmental rather than hereditary factors.

The incidence of hepatocellular carcinoma is more frequent in patients with chronic liver disease of whatever aetiology. In the Far East, necropsy series suggest that this is as high as 81% (Kubo *et al.*, 1978). In England and Wales the figure is near 61% (Sherlock, 1975), although more recently King's College Hospital has reported a figure of 75% which may be more realistic as it is based on autopsy data (Johnson *et al.*, 1978).

Hepatocellular carcinoma may be difficult to diagnose clinically. Abdominal pain or an abdominal mass are the usual presenting features but even when screening a population at risk (a group with known cirrhosis) Kubo *et al.* (1978) recorded abdominal pain in only 55% and increase in liver size in only 25%. The development of a positive serum alphafetoprotein indicates the high probability of hepatocellular carcinoma in patients with known cirrhosis, (Johnson *et al.*, 1978). Other liver function tests are useful as prognostic indicators (Cochrane *et al.*, 1977; Primack *et al.*, 1975) but are not specific diagnostic indicators of hepatocellular carcinoma. An elevated serum alphafetoprotein is seen in about 85% of hepatomas, using sensitive tests (*i.e.* radioimmunoassay). An elevated AFP may however be seen occasionally with any cirrhosis and with hepatic metastases. It may also occur in acute liver disease although this latter should not present a diagnostic problem. Plasma carcinoembryonic antigen may be elevated in hepatocellular carcinoma but considerable overlap occurs with cirrhosis (Richart *et al.*, 1979). Imaging procedures such as isotope hepatic scintigraphy, ultrasound or CT scanning either alone or in combination detect the tumours. Grey scale ultrasound has been successfully used to demonstrate and characterize space occupying lesions within the liver.

Most reported series of ultrasound demonstration of intrahepatic tumour reflect the great preponderance of metastatic lesions. Four ultrasonographic patterns of intrahepatic tumour have been described: echofree, echogenic, bullseye and mixed. To this has been added a diffuse type with disordered liver parenchyma and an enlarged liver.

Up to the time of the preparation of material for this paper we were unable to find a report of the grey-scale ultrasound appearance of primary hepatocellular carcinoma. Recently Boultbee (1979) described 30 patients with hepatoma and suggested that a large irregular highly echogenic lesion is very suggestive of a primary hepatocellular carcinoma. Sixty-seven per cent of his cases were described as echogenic. If an echogenic lesion were characteristic of hepatoma then it would allow the specific diagnosis of this tumour in the proper clinical setting.

Two further articles have appeared in American literature; one by Kamin *et al.* (1979) describing the ultrasound scan appearances in 17 primary hepatocellular tumours and two hepatoblastomas, and one by Broderick *et al.* (1980) describing, in a retrospective study, the differences and accuracy between ultrasound scans and radionuclide scans. Kamin described echogenic, diffuse disease and a mixture of these two patterns. Broderick described echogenic, echofree and disorganized parenchymal patterns.

---

*Present address: Visiting Assistant Professor, Division of Diagnostic Ultrasound, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA.

Here we report the ultrasound findings in a predominantly European population with primary hepatocellular carcinoma. The appearances are compared with those previously described for both metastatic disease and for hepatocellular carcinoma. The relationship between cirrhosis, elevated alphafetoprotein, and the presence of hepatitis B antigen in the circulation and the ultrasonographic appearance is examined and the value of grey scale ultrasound scanning as a specific diagnostic tool in intrahepatic tumour is assessed.

MATERIALS AND METHODS

Thirty-two patients who presented to the Liver Unit at King's College Hospital with suspected primary hepatocellular carcinoma on the basis of serology and a clinical suspicion were referred for ultrasound examination. The examination was performed prior to any treatment and usually prior to liver biopsy. Alphafetoprotein (AFP) was detected in serum using a sensitive radioimmunoassay technique which gives values of 2–10 mg/ml in normal healthy subjects (Johnson *et al.*, 1978); hepatitis B surface antigen (HBs Ag) was detected in serum using a radioimmunoassay technique (Abbott).

The diagnosis of primary hepatocellular carcinoma was confirmed by histology in all but one patient. In this patient the diagnosis was made on the basis of typical angiographic findings and markedly elevated serum alphafetoprotein.

Scans were performed using Nuclear Enterprises (EMI) 4200 with grey-scale scan convertor. Most cases were examined with a 2.25 MHz transducer, although more recent cases have been examined using a medium internal focus 3.5 MHz transducer.

Longitudinal, transverse and compound transverse scans were performed. The scans were reported at the time of examination. The number, size and definition of the margins of the lesion, the intrahepatic lobar distribution and the predominant echo pattern were recorded. Also associated features such as evidence of dilated intrahepatic bile ducts or ascites at the time of examination were recorded.

RESULTS

Of the 32 patients there were 27 males and five females. Their ages ranged from 19–73. In one of the male patients it proved impossible to visualize the liver adequately in spite of attempts on two separate occasions.

Of the 31 patients in whom the liver was adequately demonstrated, 17 were British, five were from other European countries, four were West Indians: two were from the Middle East and one each from the U.S.A, Rhodesia and Hong Kong. Eighteen patients had an elevated alphafetoprotein, and 11 patients had a positive HBs Ag.

Subsequent histopathology revealed that hepatocellular carcinoma was histologically well differentiated in 26 cases and poorly differentiated in the remainder. There was co-existent cirrhosis in only 13 of the patients. Of the five female patients three had used the contraceptive pill over a long period. None of the five women demonstrated elevated AFP and only one had pre-existing cirrhosis.

Four distinct ultrasonographic patterns were recognized:

Type A. Rounded, usually well-defined lesions with predominantly low-level echoes but with several scattered internal echoes, particularly recognized at higher gain (Fig. 1).

Type B. Predominantly echogenic lesions with poorly defined irregular margins and without definite shape (Fig. 2).

TABLE I

RESULTS

Ultrasonographic pattern	Lobar distribution			Well defined margins	Multiple lesions	Elevated AFP	HbS Ag positive	Cirrhosis	Male:female ratio
	R. only	L. only	Both						
A. 14 patients	9	None	5	12	6	10	6	6	13:2
B. 7 patients	1	None	6	None	All infiltrating ? Confluent	4	3	5	6:1
C. 5 patients	1	None	4	4	2	1	1	1	3:2
D. 4 patients	0	None	4	None	All infiltrating ? Confluent	3	1	1	4:0

A = Echofree; B = Echegenic; C = Mixed; D = Diffuse infiltrate.

Type C. Mixed lesions with areas of low-level echoes and areas of high echogenicity. The margins of the lesions were usually well-defined (Fig. 3).

Type D. A diffuse abnormality of liver parenchyma. The echo pattern was difficult to describe in terms of relative echogenicity because of the absence of normal liver parenchyma for comparison (Fig. 4).

The incidence of ultrasonographic pattern and their relationship to other investigations are shown in Table I. The numbers refer to numbers of patients rather than numbers of lesions.

DISCUSSION

In a review of the methods of investigation of hepatic tumours Conn (1976) expressed the hope that on ultrasound examinations hepatoma may appear echofree in an echo-opaque cirrhotic liver.

It has not so far proved possible with current technology to correlate specific ultrasound appearances with specific tumour histology. Thus although metastases from colonic or urogenital primary have been consistently associated with echodense lesions (Cosgrove and McCready, 1978) other ultrasonographic patterns do not appear to be so specific.

Boultbee (1979) has suggested that an enlarged liver with an irregular ill-defined echogenic lesion is highly suggestive of primary hepatocellular carcinoma. This is in accordance with the findings of

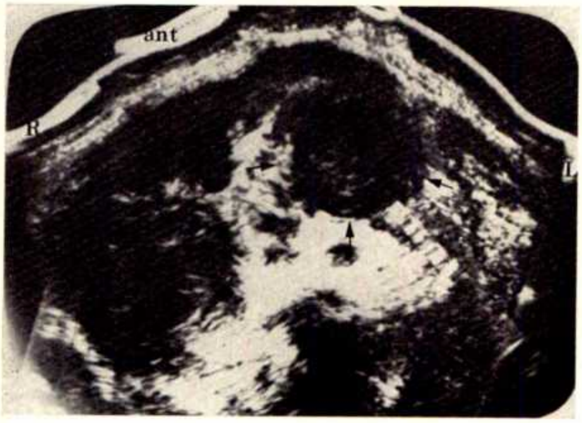


FIG. 1.

Transverse scan through the liver at the level of the hilum demonstrating a predominantly echofree tumour in a 36-year-old caucasian female.

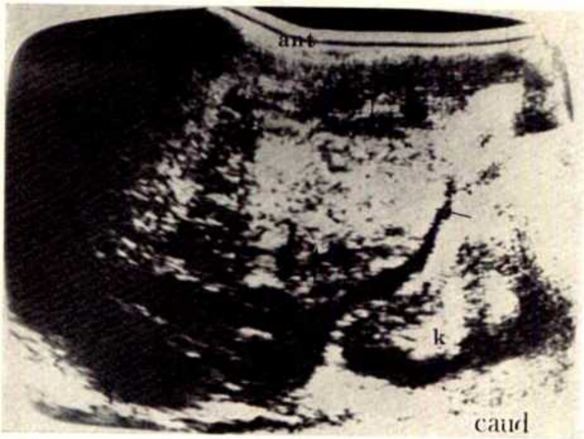


FIG. 2.

Longitudinal scan of the right lobe of the liver, with type B (predominantly echodense) tumour outlined in a 58-year-old caucasian male.

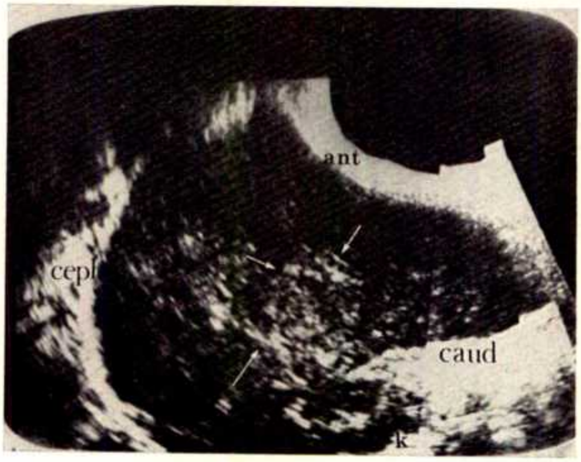


FIG. 3.

Longitudinal scan of the right lobe of the liver with type C (mixed echodensities) tumour in a 61-year-old caucasian male.

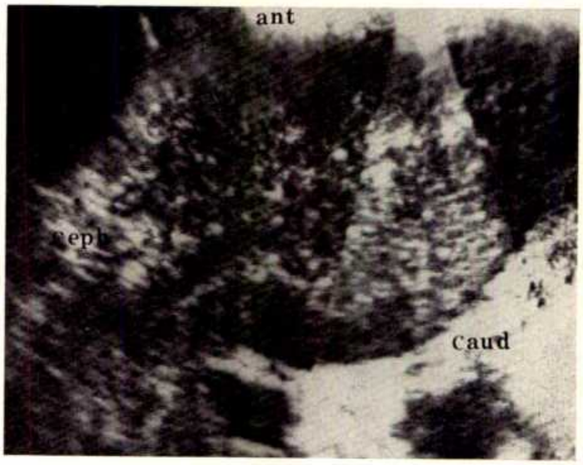


FIG. 4.

Longitudinal scan of the right lobe of liver demonstrating a diffusely abnormal liver in a 51-year-old caucasian male.

Kawasaki *et al.* (1978) who reported the bistable appearances of primary liver tumour and demonstrate a prepronderance of solid lesions (which we interpret as echodense).

The findings of this present study would not appear to confirm this. Of 32 primary hepatocellular carcinomas examined, 47% exhibited type A lesions as described and only 23% a similar pattern to that which Boultbee described as predominant. Seventeen per cent were mixed, 13% diffusely infiltrative.

In fact, rather than suggesting that ultrasound produces appearances specific of primary tumour, the incidence of ultrasound pattern in the present series is remarkably similar to that encountered by other workers for hepatic metastases. For instance, Scheible *et al.* (1977) report an incidence of 37% for bullseye lesions and 28% with a mixed pattern. Similarly the work of Green *et al.* (1977) showed 30% echogenic lesions, 23% relatively echofree and 35% mixed.

It is not clear why the results of the present series should be at variance with those previously reported. Certainly the incidence of cirrhosis in this group of patients is lower than might be predicted even for a predominantly European population. This may well be due to sampling, as it does not reflect the breakdown of all liver unit patients with hepatomas. At only 41%, it is considerably lower than the expected incidence in patients from the East from whence other reports have come. Indeed in that group of patients exhibiting a dense echo pattern cirrhosis was shown to co-exist in five out of seven (71.5%) whereas in the other three groups the incidence was only 30% for group A, 20% for group C and 25% for group D respectively. There does not seem to be a significant difference in the nomenclature of these echo patterns between different papers.

It may therefore be that the apparent difference in results reflects the different incidence of co-existent cirrhosis and the effect that this has upon the ultrasonographic pattern of hepatoma. There appear no other clear correlations. The degree of histological differentiation was not reflected in the ultrasonographic pattern; nor has histologic evidence of necrosis been reflected on ultrasound (Scheible *et al.*, 1977). The age range is similar for, and there was no obvious difference in angiographic pattern between, groups A, B and C, although group D did demonstrate a very diffuse vascular abnormality.

It would appear that the irregular echogenic lesion is highly suggestive of hepatocellular carcinoma in a patient with pre-existing cirrhosis. However, there are other sonographic appearances of hepatocellular carcinoma both in the cirrhotic and non-cirrhotic patient, particularly, it seems, in Western races. The finding of a well-defined echofree lesion in the right clinical setting should also therefore suggest hepatoma.

The use of ultrasound to differentiate conclusively between primary and secondary tumour is not yet possible. With the advent of computer analysis enabling tissue characterization it may be that primary and secondary tumours will be easily differentiated. At present the value of ultrasound in hepatocellular carcinoma remains that of detection of a solid space occupying lesion in the patient at risk, the cirrhotic.

Acknowledgments

To Dr. J. W. Laws, Director of King's Radiology Department, and Dr. R. Williams, Director of Liver Unit. Many thanks to Hilary Ruddick and Jenny Beedle for support during work and to Lesley Granger for secretarial help and patience.

REFERENCES

Anthony, P. P., 1973. Primary carcinoma of the liver: a study of 282 cases in Ugandan Africans. *Journal of Pathology, 110,* 37–48.

Boultbee, J. F., 1979. Grey scale ultrasound appearances in hepatocellular carcinoma. *Clinical Radiology, 30,* 547–552.

Broderick, T. W., Gosink, B., Menuck, L., Harris, R. and Wilcox, J., 1980. Echographic and radionuclide detection of hepatoma. *Radiology, 135,* 149–151.

Cochrane, A. M. G., Murray-Lyon, I. M., Brinkley, D. M. and Williams, R., 1977. Quadruple chemotherapy versus radiotherapy: treatment of primary hepatocellular carcinoma. *Cancer, 40,* 609–614.

Conn, H. O., 1976. Nuclide scanning, ultrasound and liver biopsy in the diagnosis of hepatic tumours. Comparative evaluation of available techniques. *Clinical Gastroenterology, 5,* 665–680.

Cosgrove, D. O. and McCready, V. R., 1978. Diagnosis of liver metastases using ultrasound and isotope scanning techniques. *Journal of the Royal Society of Medicine, 71,* 652–657.

Green, B., Bree, R. L., Goldstein, H. M. and Courtney, S., 1977. Grey scale ultrasound evaluation of hepatic neoplasms: patterns and correlations. *Radiology, 124,* 203–208.

Johnson, P. J., Williams, R., Thomas, H., Sherlock, S. and Murray-Lyon, I. M., 1978. Induction of remission in hepatocellular carcinoma using Doxorubicin. *Lancet, i,* 1006–1009.

Kamin, P., Bernardino, M. E. and Green, B., 1979. Ultrasound manifestations of hepatocellular carcinoma. *Radiology, 131,* 459–461.

Kawasaki, H., Sakajuchi, S., Irisa, T. and Hirayama, C., 1978. The value of B scan ultrasound in the diagnosis of liver cancer. Accuracy compared with scintigraphy and angiography. *American Journal of Gastroenterology, 69,* 436–442.

Kubo, Y., Okuda, K., Musha, H. and Nakashima, T., 1978. Detection of hepatocellular carcinoma during a clinical follow-up of chronic liver disease. Observations in 31 patients. *Gastroenterology, 74,* 578–582.

Office of Population Censuses and Surveys, 1977. Mortality Statistics. (HMSO, London).

Peters, R. L., Afroudakis, A. P. and Tatter, D., 1977. The changing incidence of association of hepatitis B with hepatocellular carcinoma in California. *American Journal of Clinical Pathology, 68,* 1–7.

Primack, A., Vogel, C. L., Kyalwazi, S. K., Ziegler, J. L., Simon, R. and Anthony, P. P., 1975. A staging system for hepatocellular carcinoma—prognostic factors in Ugandan patients. *Cancer*, *35*, 1357–1364.

Rasmussen, S. N., Bagger, J., Wagner, F., Pedersen, J. F. and Kristensen, J. K., 1977. Ultrasonic scanning for focal liver lesions. *Danish Medical Bulletin*, *24*, 151–153.

Richard, C., Ruibal, A., Monné, J., Vilaseca, J. and Guardia, J., 1979. Carcinoembryonic antigen in liver disease. *Lancet*, *i*, 447–448.

Scheible, W., Gosink, B. B. and Leopold, G. R., 1977. Grey scale echographic patterns of hepatic metastatic disease. *American Journal of Roentgenology*, *129*, 983–987.

Sherlock, S., 1975. Hepatic tumours. In *Diseases of the Liver and Biliary System* (Blackwell Scientific Publications, Oxford), pp. 665–698.

Book reviews

Ultrasound in Medicine and Biology. Edited by T. Wagai, R. Amoto, Associate Editor, V. R. McCready, pp. xiii+281, 1980 (Excerpta Medica, Amsterdam), $63.50/D.fl.130.00. ISBN 90-219-0439-X.

This is the published proceedings of the second meeting of the World Federation of Ultrasound in Medicine and Biology which was held in Miyazaki, Japan in July 1979. It consists of 43 out of the 59 papers presented and claims to represent the latest information and developments from all over the world in the field of diagnostic ultrasound.

The contents of the book cover a wide range of clinical applications and technical aspects of ultrasound, with contributions from 15 different countries, though not surprisingly the Japanese papers are most numerous.

Having attended many such meetings in various parts of the world I have seldom found them to be a genuine reflection of the current state of the art, and certainly many of the papers presented at this meeting and published in these proceedings merely represent different peoples' clinical experiences with commercially available equipment. There is therefore nothing very new or startling in this book and, in common with most other Proceedings, this book is unlikely to be purchased by individuals, but may be a useful source of reference.

H. B. Meire.

Manual of Ultrasonography. By K. J. W. Taylor, P. Jacobsson, C. A. Talmont and R. Winters. pp. 211, 1980 (Churchill Livingstone, Edinburgh). £12·00.
ISBN 0443-08053-4

This is an excellent book which is very readable and of value for the experienced and inexperienced alike. It is well balanced and covers most forms of ultrasound examination apart from examination of the heart.

The first three chapters deal simply and clearly with basic principles, instrumentation (including real-time) and artefacts and pitfalls. Twelve separate clinical chapters follow which deal with anatomy, pathology, technique and interpretation of each subject in a clear and succinct manner. The grey-scale illustrations are excellent and are supported by helpful labelled line drawings. There is a brief bibliography at the end of each chapter.

Some points have been lost for the sake of brevity but there is a wealth of information in these 200 pages. It is essential study for all trainees in ultrasonography and is the text of choice for the radiologist or clinician who has not yet familiarized himself with this modality.

A. B. Ayers.

Measurement of the Performance Characteristics of Diagnostic X-ray Systems Used in Medicine. Part I: X-ray tubes and generators. Topic Group Report 32. pp. 29, 1980. (Hospital Physicists' Association, London), £6·00.
ISBN 0-904181-17-0

This booklet is the first of a series being produced by the Diagnostic Radiology Topic Group of the Hospital Physicists' Association. The series is designed to give practical guidance to physicists and others who are increasingly being asked to monitor the performance of X-ray systems.

Part I of the series deals with the measurement of tube output and consistency, filtration and half-value layer, exposure time, kilovoltage calibration, focal-spot size, and light-beam diaphragm alignment. For each situation, measurement techniques are recommended and described, the equipment required listed, and specifications of acceptable performance given. The latter are either European or British standards, or, where no such standards exist, recommendations made by the members of the Topic Group. An appendix sets out the results of measurements obtained from a large number of X-ray units situated in three NHS regions. These will provide the user of the booklet with a guideline to the sort of variations in performance which are found at present with X-ray equipment being used in the NHS. Finally, specimen data sheets are provided which the user may find useful when recording data taken in the field.

In my view, this is an excellent, well-produced booklet that will not only prove to be invaluable to staff monitoring the performance of diagnostic X-ray equipment, but, by its clarity and information content, will positively encourage more of such monitoring to be carried out. I look forward to subsequent publications in this series.

J. L. Haybittle.

1981, *British Journal of Radiology*, *54*, 312–317

Management of soft tissue tumours by limited surgery combined with tumour bed irradiation using brachytherapy and supplementary teletherapy

By E. E. D. Mills, B.Sc., M.B., Ch.B., M.Med. (Rad T) and E. R. Hering, Ph.D., M.I.Biol., M.Inst.P.

Departments of Radiotherapy and Medical Physics, Groote Schuur Hospital, Cape Town

(*Received July 1980 and in revised form October 1980*)

ABSTRACT

Sixteen of 17 soft-tissue sarcomas were controlled by limited resection combined with high-dose radiation therapy using brachytherapy with or without supplementary cobalt teletherapy. Function was retained with preservation of the limb in all lesions in extremities. Adjuvant chemotherapy was used in four of five pathological Grade III cases.

The now widely-accepted principle of limited surgery and high-dose radiotherapy for the local management of soft-tissue sarcomas (Gilbert *et al.*, 1975; Suit *et al.*, 1973) illustrates well the changing rôle of surgery in the management of malignant disease.

Traditionally the surgical approach to soft-tissue sarcomas has been determined by the nature and location of the lesions. Experience has shown that simple excision is associated with an unacceptable recurrence rate ranging from 75–90% (Shieber and Graham, 1962; Cadman *et al.*, 1965). Pack and Ariel (1964) advocated the more radical approach using wide excision or soft-part resection. This resulted in reduction of the local failure rate to levels of 25–40% (Shieber and Graham, 1962; Castro *et al.*, 1973). Even after total limb ablation, local failure rates as high as 18% have been reported (Cantin *et al.*, 1968).

Experience at Groote Schuur Hospital has shown that although radiation therapy alone is of limited benefit in the local control of soft tissue tumours, the occasional good response of some irresectable lesions has made possible subsequent resection with long-term local control. Similar experience has been reported by other workers (Martin *et al.*, 1976); it is experience of this nature that has led to the accepted concept of limited surgery plus high-dose radiotherapy in the management of these conditions, giving control rates of 80–90% (Suit *et al.*, 1973; Lindberg *et al.*, 1977).

The delivery of high radiation doses to the volume of interest has been made possible by the use of sophisticated megavoltage planning systems. Even so, the risk to adjacent normal tissues, resulting in sequelae such as peripheral neuropathy, soft-tissue fibrosis and interference in joint function, has imposed a limitation on the therapeutic possibilities. Ellis (1975a; b) recommended localized implantation of the tumour bed with radioactive sources delivering a high dose locally with a rapid fall off with distance, affording protection to nearby normal tissues. Any resulting deficiencies in dosimetry can be corrected with supplementary external beam therapy. This technique has been found to be particularly valuable in a small group of patients presenting with soft-tissue tumours found at operation to be so intimately related to adjacent vital structures as to render gross local excision impossible. This paper reports the experience with a group of patients managed in this way.

CASE MATERIAL

From 1975 through to 1979, 200 patients with soft-tissue sarcoma were registered through the Groote Schuur Hospital sarcoma clinic. Patients were staged according to the recommended system of the American Joint Committee for Cancer Staging and End Result Reporting (Russell *et al.*, 1977). Seventeen patients seen pre-operatively were considered suitable for entry into the study according to the following criteria.

(1) Accessibility of the site, namely: upper limb (four patients), lower limb (five patients), head and neck (three patients), chest wall (two patients), back and buttock area (four patients).

(2) Lesions greater than 5 cm diameter; or

(3) Close proximity to vital structures, namely, bone, nerves and blood-vessels, rendering radical excision impossible regardless of size or grade of the tumour; or

(4) Recurrent lesions following previous excision.

(5) Metastasis-free.

Case records of the 17 patients were analysed with respect to age, tumour site, size, stage, histology, the time-dose fractionation (TDF) factors achieved, adjuvant chemotherapy, complications, follow-up and disease status (Table I).

Address for reprints: Dr. Elwin E. D. Mills, Radiotherapy Department, Groote Schuur Hospital, Observatory 7925, Cape Town, South Africa.

TABLE 1

TUMOUR SITE, SIZE, CLINICO-PATHOLOGY, TDF FACTORS USED, COMPLICATIONS AND FOLLOW-UP OF THE 17 CASES

No	Histology	Site	Size (cm)	Clinico/path. T. G. stage	TDF			Radiation complications	Follow up		
					Brachytherapy	Teletherapy	Total		Months	Status	Remarks
1	Synovial Sa.	Elbow	4 × 2, 5	3 2 IVa	50	80	130	Skin breakdown	58	NSR	Good function
2	Neuro-fibro Sa. Recurrent	Chest wall	16 × 16	3 2 IVa	154	Nil	154	—	53	NSR	Good function
3	Neuro-fibro Sa. Recurrent	Neck & chest	6 × 4	3 1 IVa	93	42	124	—	52	NSR	Good function
4	Aggressive fibromatoses	Deltoid	8 × 6	2 1 Ib	100	Nil	100	—	52	NSR	Good function
5	Myxolipo Sa.	Thigh	6 × 6	2 2 IIb	100	50	134	—	30	NSR	Good function
6	Aggressive fibromatoses	Neck	9 × 8	3 1 IVa	79	62	135	—	30	NSR 2	Good function LTFU
7	Epitheloid Sa.	Palm	2 × 2	3 2 IIa	100	Nil	100	—	33	NSR	Good function
8	Malignant histio Sa.	Knee	7 × 5	2 2 IIb	66	70	129	—	30	NSR	Good function
9	Aggressive fibromatoses	Deltoid	8 × 8	3 1 IVa	65	44	91	—	10	NSR	Reduced function 30 mo LTFU
10	Aggressive fibromatoses	Back	19 × 12	3 1 IVa	51	65	109	—	30	NSR	Good function
11	Fibro Sa.	Palate	1, 5 × 1	1 3 IIIa	78	37	98	—	22	NSR	Good function Thoracotomy and cytotoxic therapy for mets at 9 mo. NED
12	Recurrent neuro fibro Sa.	Back	6 × 4	2 2 IIb	65	83	144	—	20		Rec. 9 mo. Salvage excision NED 20 mo.
13	Lipo Sa.	Back	12 × 10	3 3 IVa	34	73	102	—	18	NSR	AT. NED
14	Aggressive fibromatoses	Chest wall	12 × 8	3 1 IVa	56	62	111	—	12	NSR	Good function
15	Rhabdomyo-Sa.	Thigh	10 × 8	2 3 IIIb	61	53	109	—	10	NSR	AT. Pulmonary mets at 10 mo.
16	Malignant histio Sa.	Lower leg	12 × 12	2 3 IIIb	45	49	85	Shed 50% skin graft	10	NSR	AT. NED
17	Synovial Sa.	Lower leg	7 × 7	2 3 IIIb	53	68	111	Wound breakdown	7	NSR	AT. NED

Key: LTFU = Lost to follow up; NSR = No sign of recurrence; AT = Adjuvant chemotherapy (Vincristine, Methotrexate with citrovorum rescue, Endoxan, Adriamycin); REC = Recurrent tumour; NED = No evidence of disease.

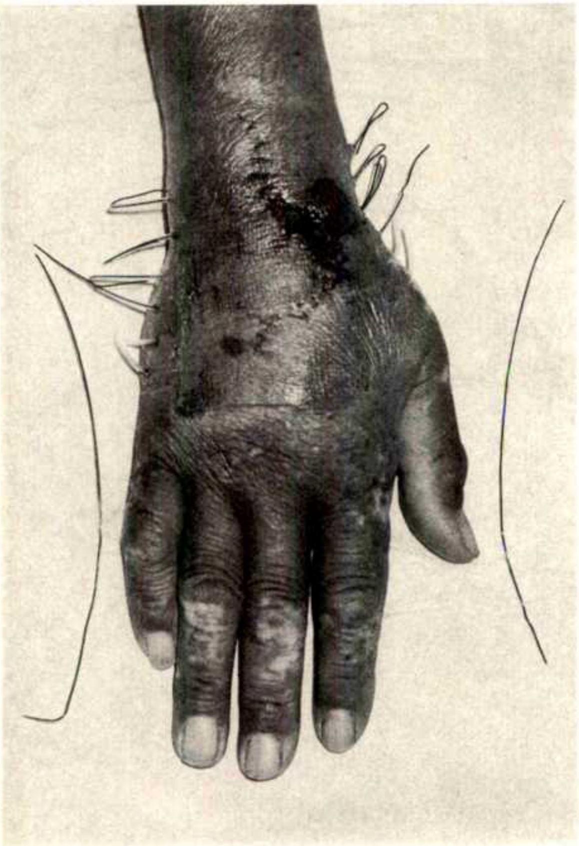


Fig. 1.
Showing outer tubes *in situ*. Lumen patency maintained using malleable wire inserts.

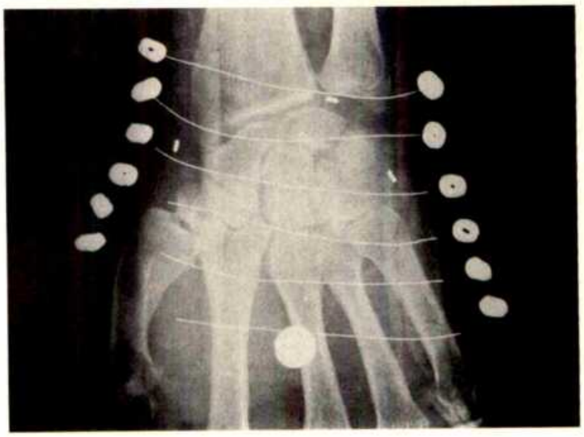


Fig. 2.
Radiograph showing ^{192}Ir wires located in relation to opaque markers inserted into limits of tumour bed.

Tumour histogenesis and stage

Whilst five of 17 tumours were classified histologically as aggressive fibromatoses, the remaining 12 represented a fair cross-section of tumours seen. Five patients had pathological Grade III lesions, four received adjuvant chemotherapy for periods ranging from nine months to one year, three remain well while one developed pulmonary metastasis at ten months. One other patient with a Grade III lesion of the palate did not receive adjuvant therapy and suffered a relapse of peripheral disease with pulmonary metastases at nine months.

Brachytherapy: implant vs. applicator

Fourteen of 17 patients were considered suitable for interstitial implant of the exposed tumour bed. Three patients in whom the tumour bed had been covered by a split skin graft were considered to be more suited to a surface applicator.

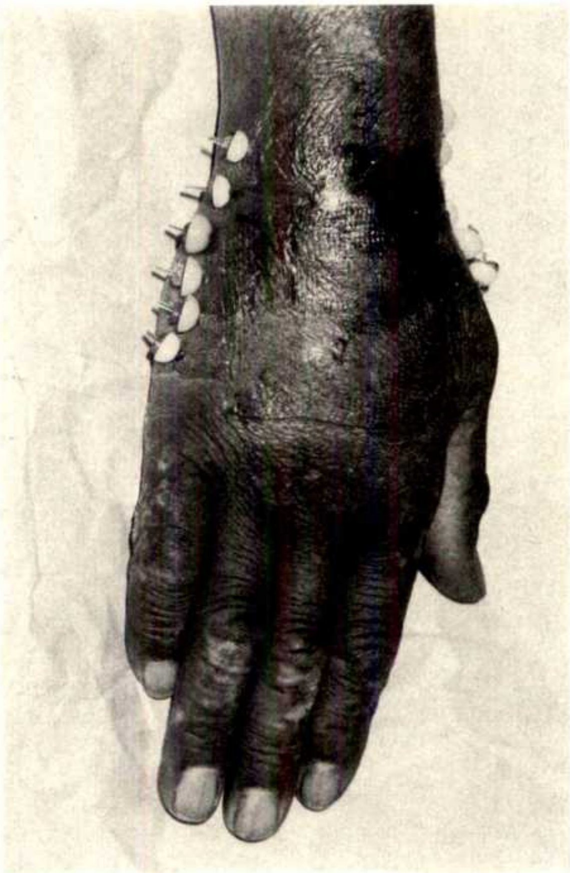


Fig. 3.
Position of afterloaded tubes maintained using nylon collars secured with lead crimps.

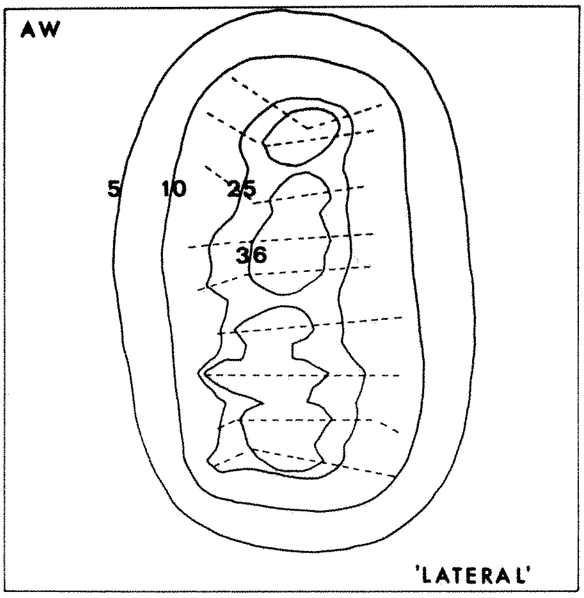


FIG. 4.
Lateral dosimetric plane for patient 17. The dotted lines indicate the position of the iridium wires. The tumour bed was treated to the 25 cGy (rad) hr^{-1} line.

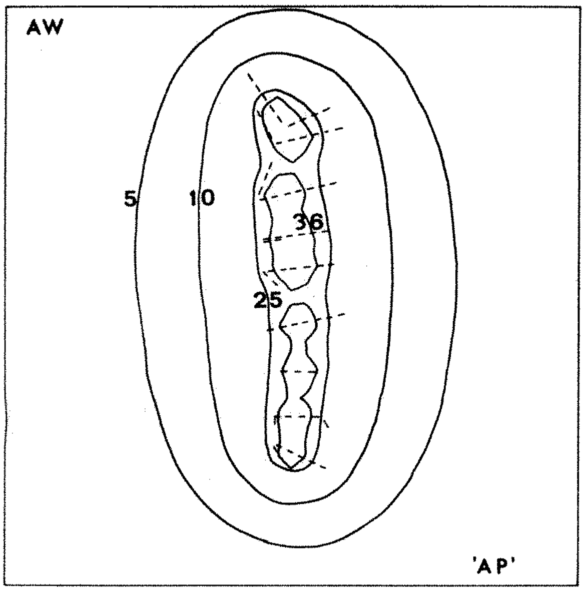


FIG. 5.
AP dosimetric plane for the patient shown in Fig. 4.

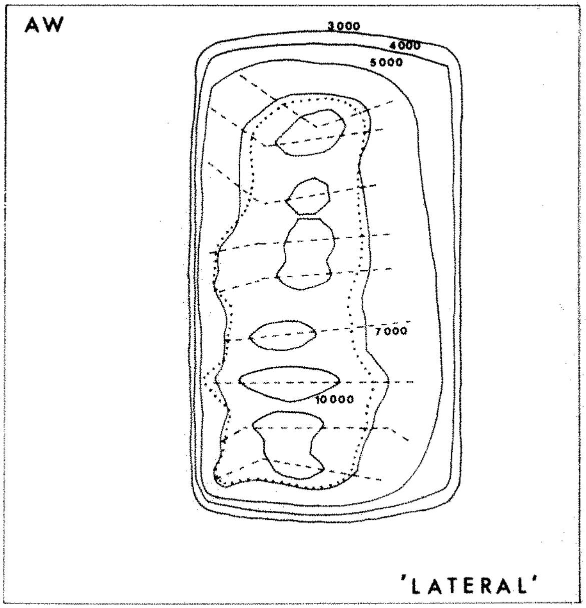


FIG. 6.
Lateral dosimetric plane showing the summated dose distribution for the implant and external beam therapy. The dotted line indicates the volume treated by the implant. The line indicating the total tumour dose of 7000 cGy (rad) follows very close to this line.

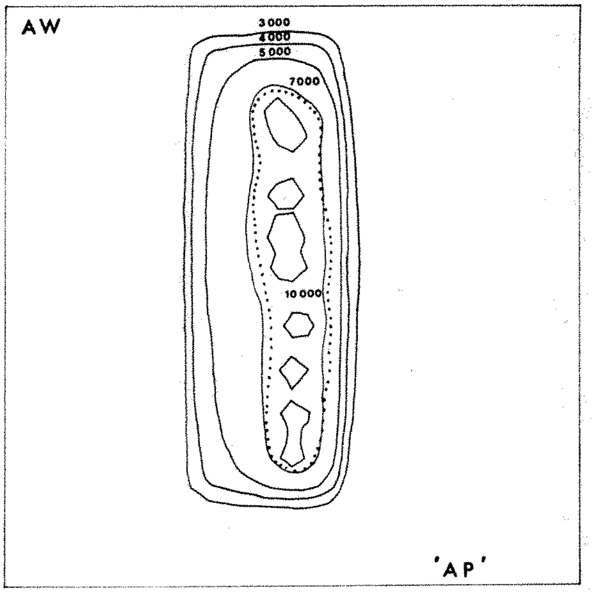


FIG. 7.
As for Fig. 6 but in the AP plane.

Supplementary telecobalt therapy

Fourteen of the 17 patients received supplementary telecobalt therapy which was aimed to deliver between 40% and 60% of the total radiation in the plane of the tumour bed. Because of ideal radiation dosimetry the remaining three tumours received brachytherapy only.

Methods

Surgery

Close proximity of tumour to the vital structures permitted only limited excision. In nine of 17 patients only reduction in tumour bulk was permissible with gross disease left *in situ*. The remaining eight patients all had microscopic evidence of residual tumour. The limits of the tumour bed were marked with silver clips.

Interstitial implant

The technique used has been well described by Paine (1972) while the implant geometry followed the formula of Ellis (1975b). The after-loading was accomplished on the 10th to 14th post-operative day, ensuring adequate coverage of the tumour bed as outlined radiographically by metal markers (Figs. 1 and 2). Retention of the tubes was maintained using lead crimps separated from the skin by nylon collars (Fig. 3).

Surface applicators

These were used in three patients in whom the tumour bed had been covered by split skin. In two, radium moulds were made in accordance with the rules of Paterson and Parker (1938). The third patient had a surface applicator held continuously in position in the form of a dressing on the lower leg.

Dosimetry

Using a TP-11 planning computer, a dose distribution was calculated from AP and lateral radiographs of each of the implants and moulds. A typical computer-generated dose-distribution is seen in Figs. 4 and 5, from which the dose rates for the treatment were selected. Dose rates at 1 cm ranged from 17 to 65 cGy (rad) per hour.

A typical summated dose distribution for the combination of external beam and brachytherapy is shown in Figs. 6 and 7 and indicates a uniform dose gradient through the tumour bed. The dotted line corresponding to the 7000 cGy (rad) isodose delineates the tumour limits. Fourteen of the 17 patients were treated with the combined modalities. Two patients had ideal dose distributions through the implants and received no supplementary teletherapy. One patient had mould application only.

Dosage

A total dosage to a point 1 cm from the plane of the implant sources was estimated from the TDF tables of Orton and Ellis (1973). A decay-corrected TDF of 125 to 135 from the combined modalities was considered optimal. Where the full treatment was given through the implant alone, a TDF of 95 to 100 was aimed at.

The TDF contribution from the implant ranged from 40%–100% depending on the suitability of the distribution. Generally, however, it is aimed to give half the treatment through brachytherapy and half with teletherapy.

Results

Two patients, both with tumours classified as aggressive fibromatoses, have been lost to follow-up at 30 and 10 months. Neither patient showed evidence of disease when last seen. The remaining 15 patients have been followed up for periods ranging from seven to 58 months (mean 28 months). The degree of control of local disease has been of a high order with only patient No. 12 manifesting a recurrent neurofibrosarcoma of the back at nine months. The recurrence was small and amenable to local excision with no further evidence of disease at 20 months. Pulmonary metastases were seen in two cases, both with pathological Grade III tumours. One patient (No. 11) with a palatal fibrosarcoma remains well nine months after irradiation of the whole lung, chemotherapy and resection of metastases. Disease developed in the lung of a second patient who discontinued adjuvant chemotherapy after three courses because of severe pancytopenia. Three other patients with high grade tumours on adjuvant therapy remain disease-free at 7–18 months.

Radiation complications

These were a problem in three cases. One patient had a wounded dehiscence and a second patient shedded 50% of a split skin graft. Both were lesions of the lower leg. A third patient had severe wet desquamation following the external beam component to the cubital fossa at a TDF of 129, but followed by satisfactory healing of the skin. There have been no instances of neuropathy or peripheral vascular complications. This was considered most gratifying in view of the close proximity to such vital structures in many of the cases. Subcutaneous fibrosis which manifested in four patients has not markedly interfered with function.

Discussion

All the patients in this study are alive with control of local disease; although the numbers are small and the mean follow-up 28 months, the occurrence of only one local failure is indeed promising. Collins *et al.* (1976), using a similar treatment programme, reported a 34% local recurrence rate. Their planned dose of approximately 6000 cGy (rad) to a point 0.5

cm from the plane of the implant was considerably less than in the present series. They comment that tumour-bed implant is unique in its delivery of the highest radiation dose to the site of greatest risk of relapse. The cosmetic and functional results are good and normal-tissue change can be kept at an acceptable level by good implant dosimetry.

Gilbert *et al.* (1975) reported a 44% recurrence rate in 24 months in a series of 142 soft-tissue tumours of corresponding histogenesis to those in this study, treated by high-dose radiotherapy after excision.

Likewise Suit *et al.* (1973) in a review of 57 patients with similarly managed tumours attained an 87% local control rate which compared favourably with that achieved in 243 cases from the M. D. Anderson Hospital and 653 from the Memorial Hospital, New York, managed by radical excision or amputation. They, however, acknowledge an appreciable complication rate in 12 cases resulting in subsequent limb ablation in six (10%). This was more so when the full width of the limb was included in the radiation fields. Our experience, and that of Collins *et al.* (1976) and Ellis (1975b), indicates that preservation of limb function is a significant benefit from the use of tumour bed brachytherapy.

The Groote Schuur Hospital sarcoma clinic has found an additional advantage in the extension of the multidisciplinary management into the operating theatre. Here, both the surgeon and his radiotherapy colleague have the opportunity to discuss and decide on the most appropriate methods of dealing with the problem. This can be expected to result in an increasing degree of pre-operative consultation between these two methods of management.

CONCLUSION

Brachytherapy, with or without teletherapy, delivering high-dose radiation to the tumour bed after simple excision of connective-tissue tumours, can give local control equivalent to that of radical excision, but with preservation of limb and function.

ACKNOWLEDGMENTS

Thanks are due to Dr. H. R. Sanders, Medical Superintendent, Groote Schuur Hospital, for permission to publish, and to the colleagues of the Department of Surgery, Groote Schuur Hospital, without whose co-operation this study would not have been possible.

The work was supported by grant No. 43306 of the Cancer Research Trust of the University of Cape Town.

Lastly we wish to thank various members of our secretarial staff for their assistance.

REFERENCES

CADMAN, N. L., SOULE, E. H. and KELLY, P. J., 1965. Synovial sarcoma: an analysis of 134 tumours. *Cancer, 18*, 613–627.

CANTIN, J., MCNEER, G. P., CHU, F. and BOOHER, R. J., 1968. The problem of local recurrence after treatment of soft tissue sarcoma. *Annals of Surgery, 168*, 47–53.

CASTRO, E. B., HAJDU, S. I. and FORTNER, J. G., 1973. Surgical therapy of fibrosarcoma of extremeties. *Archives of Surgery, 107*, 284–286.

COLLINS J. E., PAINE, C. H. and ELLIS, F., 1976. Treatment of connective tissue sarcomas by local excision followed by radioactive implant. *Clinical Radiology, 27*, 39–41.

ELLIS, F., 1975a. Connective tissue sarcoma. In *Handbook of Interstitial Brachytherapy*, Ed. B. S. Hilaris (Publishing Sciences Group, Inc., Acton, Mass.), pp. 263–273.

1975b. Tumour bed implants at the time of surgery. In *Afterloading: 20 Years of Experience, 1955–1975. Proceedings of the Second International Symposium on Radiation Therapy, New York, 1975.* Ed. Basil S. Hilaris (Memorial Sloan-Kettering Centre, New York), pp. 125–132.

GILBERT, H. A., KAGAN, A. R. and WINKLEY, J., 1975. Soft tissue sarcomas of the extremities: their natural history, treatment, and radiation sensitivity. *Journal of Surgical Oncology, 7*, 303–317.

LINDBERG, R. D., MARTIN, R. G., ROMSDAHL, M. M. and MCMURTREY, M. J., 1977. Conservative surgery and radiation therapy for soft tissue sarcomas. In *Management of Bone and Soft tissue Sarcomas: the University of Texas System Cancer Centre M. D. Anderson Hospital and Tumour Institute, 21st Annual Clinical Conference on Cancer* (Year Book Medical Publishers, Inc., Chicago), pp. 289–298.

MARTIN, R. G., LINDBERG, R. D., SINKOVICS, J. G. and BUTLER, J. J., 1976. Soft tissue sarcomas. In *Cancer Patient Care at M. D. Anderson Hospital and Tumour Institute.* Ed R. L. Clark and C. D. Howe (Year Book Medical Publishers, Chicago), pp. 473–483.

ORTON, C. G. and ELLIS, F., 1973. A simplification in the use of the N.S.D. concept in practical radiotherapy. *British Journal of Radiology, 46*, 529–537.

PACK, G. T. and ARIEL, I. M., 1964. Principles of treatment of tumours of the soft somatic tissues. In *Treatment of Cancer and Allied Diseases, Tumors of the Soft Somatic Tissues and Bone*, Ed. G. T. Pack and I. M. Ariel, 2nd ed., VIII, (Hoeber Medical Division, Harper and Row, New York), pp. 8–39.

PACK, G. T., MILLER, T. R and ARIEL, I. M., 1964. Hemipelvectomy (interilioabdominal amputation). In *Treatment of Cancer and Allied Diseases, Tumors of the Soft Somatic Tissues and Bone*. Ed. G. T. Pack and I. M. Ariel, 2nd edition, VIII (Hoeber Medical Division, Harper and Row, New York), pp. 284–302.

PAINE, C. H., 1972. Modern afterloading methods for interstitial radiotherapy. *Clinical Radiology, 23*, 263–272.

PATERSON, R. and PARKER, H. M., 1938. A dosage system for interstitial radium therapy. *British Journal of Radiology, 11*, 252 and 313.

RUSSELL, W. O, COHEN, J., ENZINGER, F., HAJDU, S. I., HEISE, H., MARTIN, R. G., MEISSNER, W., MILLER, W. T., SCHMITZ, R. L. and SUIT, H. D., 1977. A clinical and pathological staging system for soft tissue sarcomas. *Cancer, 40*, 1562–1570.

SHIEBER, W. and GRAHAM, P., 1962. An experience with sarcoma of the soft tissues in adults. *Surgery, 52*, 295–298.

SUIT, H. D., RUSSELL, W. O. and MARTIN, R. G., 1973. Management of patients with sarcoma of soft tissue in an extremity. *Cancer, 31*, 1247–1255.

1981, *British Journal of Radiology*, *54*, 318–324

Misonidazole as a radiosensitizer in the radiotherapy of glioblastomas and oesophageal cancer. Pharmacokinetic and clinical studies

By *P. Tamulevicius, B.Sc., Ph.D., †M. Bamberg, Dr. med., †E. Scherer, Dr. med. and
*C. Streffer, Dipl.-Chem., Dr. rer. nat.,

*Institut für Medizinische Strahlenphysik und Strahlenbiologie, and †Strahlenklinik und Poliklinik,
Universitätsklinikum Essen, F.R.G.

(Received August 1980 and in revised form October 1980)

ABSTRACT

Since May 1978 the hypoxic-cell radiosensitizer, misonidazole (MIS), has been under clinical investigation in a phase III trial with multiple doses of the drug in 11 patients with brain tumours (seven glioblastomas, four recurrent brain tumours) and three patients with oesophageal carcinoma. The doses of MIS administered were usually well tolerated but the principal toxicities observed were peripheral neuropathy as well as nausea and vomiting in the glioblastoma patients. The neuropathy was completely reversible. The incidence of neuropathy was not related to the pharmacological parameters of plasma level or half-life. Pharmacological assessment by high-pressure liquid chromatography included assays of plasma, urine and cerebrospinal fluid. The demethylated product, Ro–05–9963, was detected as the major metabolite. Peak plasma levels were obtained one to four hours after administration of MIS, with a half-life of five to ten hours. Cerebrospinal fluid levels of MIS correlated well with those of the plasma. MIS was mainly excreted as the demethylated metabolite, but less than 40% of the given dose could be recovered. The results obtained suggest that the present MIS dosage for glioblastoma patients results in a low plasma level with no observable therapeutic effect.

The use of electron-affinic substances as radiosensitizers in the radiotherapy of solid tumours is based on their ability to sensitize the relatively radioresistant hypoxic cells which may be responsible for reduced radiocurability of tumours (Fowler *et al.*, 1972). The 2-nitroimidazole derivative, misonidazole (Ro–07–0582; MIS) has been shown to be an effective radiosensitizer from *in-vitro* and *in-vivo* experimental studies (Adams *et al.*, 1978; Denekamp and Fowler, 1978). It appears to be one of the most promising drugs of its kind available for clinical use (Fowler *et al.*, 1976) and extensive trials are currently under way at various centres to assess its usefulness in the radiotherapy of human tumours (Dische *et al.*, 1977; Saunders *et al.*, 1978; Wiltshire *et al.*, 1978). These studies have emphasized the importance of the pharmacokinetics of MIS in relation to its toxic and therapeutic effects. This report describes our experiences of a phase III clinical trial in Essen with patients undergoing radiation therapy for cerebral gliomas, oesophageal carcinoma and recurrent brain tumours after receiving multiple fractions of MIS. A preliminary account of this work has already been reported (Bamberg *et al.*, 1980).

PATIENTS AND METHODS

Since May 1978 14 patients with high-grade gliomas, oesophageal cancer or recurrent brain tumours were treated with multiple doses of misonidazole. The first group of seven patients with cerebral gliomas (Grade III-IV) received concomitant daily fractionated irradiation three to four hours after administration of drug. 40 Gy (4000 rad) was given to the whole brain from a telecobalt machine (2 Gy (200 rad), five times a week) using lateral opposed fields, followed after a two-week interval by a booster dose of 20 Gy (2 Gy, five times a week) to the tumour region from a 6 MeV linear accelerator. MIS was administered as 500 mg or 100 mg tablets in 30 single doses standardized to 400 mg/m^2. Total doses of MIS ranged from 18–24 g in those patients surviving the whole course of treatment.

In the second group, three patients with oesophageal squamous-cell carcinoma were irradiated from a linear accelerator to a total tumour dose of 30 Gy given in ten fractions of 3 Gy each four times a week. Three to four hours before treatment a MIS dosage of 1 g/m^2 to a total dose of 18–19 g was given. After this combined treatment schedule, further irradiation without MIS was carried out to tumour doses between 60 and 70 Gy.

In addition four patients with recurrent brain tumours—two medulloblastomas, one astrocytoma and one pinealis tumour—received radiation therapy in ten fractions to doses of only 20 Gy because of previous irradiation. Prior to this limited irradiation single doses of 1 g/m^2 MIS were delivered to a total dose of 17–18 g.

All patients with brain tumours were maintained on dexamethasone throughout the treatment. All

---

Address for correspondence: P. Tamulevicius, Institut für Medizinische Strahlenphysik und Strahlenbiologie, Universitätsklinikum Essen, Hufelandstr. 55, D–4300 Essen 1, F.R.G.

additional medication given to the patients during therapy was recorded. The following substances were excluded from the study: other nitroimidazoles, aminoglycosides, nalidixic acid, isoniazides and barbiturates. Assessment was made on the basis of neurological function, gastrointestinal tolerance, skin reaction and survival time. Computerized axial tomography for brain-tumour patients and radiographs of the oesophagus for patients with oesophageal cancer were the main follow-up examinations. Laboratory investigations of complete blood counts, liver enzymes, electrolytes, creatinine, uric acid and urine analysis were repeated at regular intervals.

Plasma samples

At the start of these trials, whole blood was collected with citrate once a week at the time of administration of MIS (zero hours), of irradiation (three to four hours after administration, taken as the time to obtain peak plasma levels), as well as 12 hours and 24 hours later. Subsequently, in order to obtain more detailed pharmacokinetic data, blood was collected from patients at hourly intervals for the first 12 hours and finally 24 hours following oral administration of MIS. Plasma was obtained by centrifugation (2000 g for ten minutes), frozen and stored at −20°C.

Urine samples

Urines were collected over 24 hour periods twice a week from each patient and stored at −20°C.

Cerebrospinal fluid (CSF)

CSF samples were collected only once, five to six hours after oral administration of MIS, on the final day of the therapy schedule from high-grade glioma patients only, and stored at −20°C.

High-pressure liquid-chromatography determination

Plasma, urines and CSF were analysed by reversed-phase high-pressure liquid-chromatography (HPLC) as described by Workman *et al.* (1978a), except that the mobile phase was 12% methanol/water and using a Nucleosil C_{18} column (25 cm × 4 mm I.D., particle size 10 μm, Macherey and Nagel, Düren, F.R.G.). Eluents were monitored at 335 nm. This method allowed for the specific determination of MIS and its O-demethylated metabolite, Ro-05-9963. Preliminary studies showed that the concentrations of MIS and Ro-05-9963 were identical in whole blood and plasma. Complete recovery of both drugs from plasma, urine and CSF was obtained. Peak areas were quantitated by means of a Dia-log integrator (Düsseldorf).

RESULTS

Clinical

Three of the seven patients with high-grade glioma developed a peripheral sensory neuropathy. These neurological symptoms affecting feet and hands were mild, whereas one patient (patient S; Table I) also had convulsions during treatment in spite of dexamethasone. The neurotoxicity occurred after more than 15 g of MIS and disappeared completely within two weeks after completion of radiotherapy. Four patients in this group experienced slight nausea and one male patient (K) suffered from additional transient vomiting in the first two weeks of combined treatment. One female patient (H)

TABLE I

Toxicity of misonidazole in seven patients with high grade glioma (400 mg/m^2—60 Gy/6 weeks—30 fractions × 2 Gy)

Patient	Sex	Age	Neuropathy	Nausea or vomiting	Skin reactions	MIS (total dose g)	Survival time (months)
M	f	65	—	M	—	4.2	intercurrent, died (pulmonary embolism)
K	m	45	—	S	—	13.6	intercurrent, died (tumour growth)
L	f	68	M	M	—	21	3, died (circulatory failure)
H	f	65	M	—	M	21	6, died (circulatory failure)
B	f	64	—	—	—	18	9, died (local recurrence)
S	f	46	S	M	—	18	12, died (local recurrence)
La	m	44	—	—	—	24	7, NED.

M = mild symptoms; S = severe symptoms; NED = No evidence of disease.

TABLE II

MISONIDAZOLE PHASE III STUDY RESULTS (HIGH GRADE GLIOMA)

Patient			Peak plasma conc. (μg/ml)		Half-life ($T_{\frac{1}{2}}$) h	CSF conc. (μg/ml)	
Glioma	Sex	Age	Ro-05-9963	Ro-07-0582		Ro-05-9963	Ro-07-0582
M	f	65	7.1	18.2	8.0	—	—
K	m	45	5.7 (4.6-6.0)	12.4 (10.3-13.4)	5.2	—	—
L	f	68	3.4 (2.5-6.2)	37.4 (27.8-45.8)	8.0	1.3	33.8
H	f	65	4.8 (4.2-5.7)	27.7 (20.3-34.7)	6.8	1.4	3.3*
B	f	64	2.4 (1.6-3.2)	18.1 (13.5-22.8)	5.4	4.6	24.4
S	f	46	5.2 (3.7-8.6)	17.5 (13.9-21.0)	6.2	2.2	20.0
La	m	44	2.3 (1.8-2.8)	12.6 (10.0-14.9)	5.6	1.0	11.0

*Sample obtained 24 h after application of MIS.

TABLE III

TOXICITY OF MISONIDAZOLE IN SEVEN PATIENTS (THREE OESOPHAGEAL CANCER, FOUR RECURRENT BRAIN TUMOURS)

Patient	Sex	Age	Neuropathy	Nausea or vomiting	Radiotherapy (Gy/ fractions)	MIS (total dose g)	Survival time (months)
Oesophageal cancer							
C	m	49	—	M	30/10*	19	6, died (liver metastases)
P	m	58	—	—	30/10†	18	9, died (local failure)
Ka	m	51	—	M	30/10†	18	NED.
Recurrent brain tumour							
Medulloblastoma							
Kr	f	18	—	—	20/10	18	1, died (local recurrence)
Mu	m	27	—	M	20/10	18	9, NED.
Astrocytoma							
R	f	37	—	—	20/10	17	11, NED.
Pinealis tumour							
F	f	34	—	—	20/10	17	6, living, but tumour progression

NED = No evidence of disease; * = +40 Gy without MIS; † = +36 Gy without MIS; M = mild symptoms.

developed a mild maculopapular erythema after a MIS dosage of 12 g, without fever or pruritus, appearing on the abdomen and spreading to back, legs and arms. A distinct regression of this disseminated rash could be observed after three days; as this interval occurred during a weekend the medications could be continued without delay. This patient did not receive any "unallowed" medication which could have been related to the skin rashes.

Two patients died intercurrently of tumour growth and pulmonary embolism and two other patients because of circulatory failure. In the latter cases no signs of recurrences could be identified in a CT scan, but their good general condition had worsened during combined treatment and had not returned to the level before therapy. After a follow-up period of nine and 12 months, two patients died of local recurrence, while one patient is still alive seven months after therapy (Karnofsky: 90%). Autopsies were carried out only in the first two cases of intercurrent death without demonstrating special histological signs caused by MIS. The three patients with oesophageal cancer of the second group and the four patients with recurrent brain tumours, who received a higher MIS dose of 1 g/m^2, showed no neurological side effects apart from mild nausea in three cases. Two patients with oesophageal carcinoma died of liver metastases or after surgery for local recurrence, whereas one male is alive with no evidence of disease (NED) five months after therapy. In the young patients Kr and Mu (Table III) with recurrent medulloblastoma only 20 Gy were delivered in combination with MIS, because 30 Gy to the whole cerebrospinal fluid had been administered previously. The young girl died of local recurrence one month after radiotherapy; the other patient is

TABLE IV

MISONIDAZOLE PHASE III STUDY RESULTS (OESOPHAGEAL AND RECURRENT BRAIN TUMOURS)

Patient	Sex	Age	Peak plasma conc. (μg/ml)		Half-life ($T_{\frac{1}{2}}$) h
			Ro–05–9963	Ro–07–0582	
Oesophageal cancer					
C	m	49	5.3	65.5	10.0
P	m	58	5.1 (3.4–7.0)	27.0 (27.0–27.0)	7.2
Ka	m	51	2.0 (1.2–2.8)	32.4 (30.7–34.0)	8.8
Recurrent brain tumour					
Medulloblastoma					
Kr	f	18	1.8 (1.6–2.0)	47.3 (46.5–48.0)	8.2
Mu	m	27	2.2 (1.8–2.7)	42.7 (39.3–46.0)	7.6
Astrocytoma					
R	f	37	7.0 (4.4–9.4)	46.0 (39.7–49.6)	6.4
Pinealis Tumour					
F	f	34	2.0 (1.7–2.2)	48.2 (42.3–55.4)	8.2

alive with NED nine months later (Karnofsky: 80%). A young female with recurrent astrocytoma received a second course of radiotherapy with MIS in spite of surgery, postoperative irradiation and 12 courses of CCNU. After a follow-up period of 11 months there are no signs of recurrence (Karnofsky: 60%). The patient with the tumour of the pineal region developed a recurrence four years after a radiation dose of 54 Gy. Six months after the second course of treatment with MIS she is alive but shows signs of tumour progression, demonstrated by CT scan (Karnofsky: 50%).

PHARMACOKINETICS

Plasma levels of MIS

The half-life ($T_{\frac{1}{2}}$) of MIS in plasma in patients receiving 400 mg/m^2 (high-grade gliomas) or 1 g/m^2 (oesophageal carcinoma and recurrent brain tumours) was found to be in the range five to ten hours as shown in Tables II and IV. Plasma levels of about 12–70 μg/ml were obtained three to four hours after administration at these doses. These levels, given as the mean with the range in parenthesis, remained relatively constant over the period investigated for each patient although large variations were obtained from patient to patient. MIS was always more concentrated in plasma than Ro–05–9963, the latter constituting up to about 20% of the MIS level, irrespective of dosage. O-demethyl metabolite levels in plasma remained relatively constant over a 24 hour period. More detailed pharmacokinetic studies showed that peak plasma levels of MIS were reached within one hour of administration and maintained a plateau level for up to four hours followed by a slow disappearance of drug from the blood over 24 hours.

Typical time curves for MIS and Ro–05–9963 are given in Fig. 1. The elimination of MIS apparently followed first-order kinetics. However, two patients, M and K, who died during therapeutic treatment, showed a large proportion of Ro–05–9963 in their plasma, 39 and 45% respectively (Table II). Both patients showed an extremely low level of total nitroimidazole in plasma, although this could not be directly related to their physical condition.

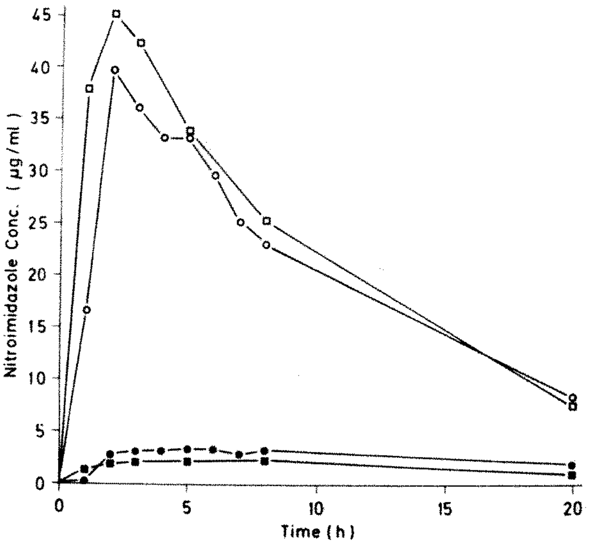


FIG. 1.

Plasma misonidazole (○, □) and demethylmisonidazole, Ro–05–9963 (●, ■) concentrations in two glioma patients (Mu: ○, ●; Kr: □, ■) after oral administration of misonidazole at 1 g/m^2.

CSF levels of MIS

CSF concentrations of Ro–05–9963 and MIS were determined in all glioma patients. The level of Ro–05–9963 was also found to be low in relation to that of MIS. MIS levels were comparable to those in plasma for all patients studied so far, reaching 80–100% of the plasma level. In the case of patient H, the CSF sample was obtained 24 h after administration of the final MIS dose. This accounts for the low level found (Table II).

Urinary excretion of Ro–05–9963 and MIS

The distribution and concentration of the O-demethylated metabolite and MIS in urine over a 24 hour period for several of the glioma patients is given in Fig. 2. The data show that extensive metabolism of parent drug occurred and that, in general, more Ro–05–9963 was excreted than MIS. The ratio of Ro–05–9963 to MIS was found to vary considerably from patient to patient and for each patient during the course of treatment. Patient H showed a ratio of approx. 1:1 almost up to the final phase of the treatment schedule but a 7:1 ratio at the end. Patient L showed a ratio of approx. 1:1 over the entire period of treatment whereas patients B, R and S showed ratios ranging from about 2:1 to 9:1. Patients M and K are particularly interesting since they excreted virtually all of the administered MIS as the Ro–05–9963 derivative. This unique pattern was not observed for any of the other patients. Patients P and C also showed ratios ranging from 2:1 to 4:1 but the patients with recurrent brain tumours showed a higher excretion of MIS, *e.g.* 1:2 (F), 1:3 (Kr), and 1:2–2:3 (Mu) (data not shown). The recovery of urinary nitroimidazoles accounted for about 40% of the administered drug in 24 hours and large differences in the recovery were observed for each patient.

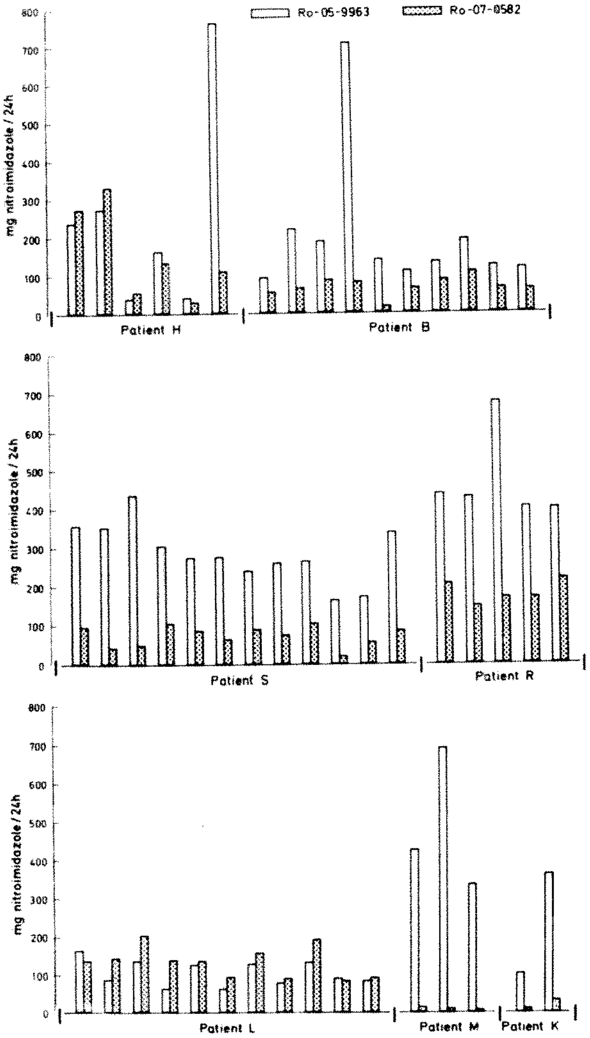


FIG. 2.

The urinary excretion of misonidazole (Ro–07–0582) and its metabolite demethylmisonidazole (Ro–05–9963) in glioma patients following oral administration of misonidazole at 400 mg/m². Patient R received 1 g/m². The abscissa shows the urine samples collected twice weekly. Bars 1+2=week 1; bars 3+4=week 2, etc.

DISCUSSION

Early trials with MIS were severely handicapped by the occurrence of neurotoxicity, especially when higher doses (over 24 g) were given (Dische *et al.*, 1977). To avoid these side effects a total dose of 12 g/m² was not exceeded. Of all patients only one developed convulsions possibly caused by MIS and no correlation could be found between the incidence of the mild neurological symptoms and the low plasma levels or total dose of MIS. The mild gastro-intestinal side effects in some patients could be diminished by antiemetics given before administration of drug. In one female patient a disseminated maculopapular rash occurred which was related to MIS, but the levels of plasma concentration of the drug were within normal limits. Some cases with similar dermatitis have been reported (Partington *et al.*, 1979; Urtasun *et al.*, 1977) using MIS or metronidazole, and such drug-related hypersensitivity may be expected in continued application of these radiosensitizers. In no patient could any significant changes in blood counts, cerebrospinal fluid or urine chemistry be observed during the combined treatment and follow-up period. Blood pressure and temperature were also normal.

The present pharmacokinetic studies with HPLC analysis have shown good absorption of MIS with peak plasma levels occurring one to four hours after oral administration. These findings substantiated the rationale for irradiating patients three to four hours after oral ingestion of MIS (Dawes *et al.*, 1978). Variations in MIS levels between patients were observed but the levels achieved at the dosages used are in good agreement with those of previous studies (Foster *et al.*, 1975; White *et al.*, 1979b; Wiltshire *et al.*, 1978).

In addition, significant plasma levels of the O-demethyl metabolite Ro–05–9963 were observed in all patients. The $T_{\frac{1}{2}}$ of MIS was in the range five to ten hours in all the patients studied so far. Again, these data agree well with those of other trials (White *et al.*, 1979b; Wiltshire *et al.*, 1978). No change in $T_{\frac{1}{2}}$ was observed either on repeated MIS administration or increased dosage. No decrease in the peak plasma levels of MIS after multiple-dose application was seen in this study as has been suggested to occur in primates via possible enzyme induction (Johnson *et al.*, 1976). Levels of MIS or Ro–05–9963 in tumour tissue were not determined in the present study because of difficulty in obtaining biopsy or autopsy material. In order to be effective *in vivo*, MIS must be present in the hypoxic cells in the tumour and to reach the brain would have to cross the blood-brain barrier and then penetrate into the CSF. Data from studies on the penetration of MIS into tumours (Wiltshire *et al.*, 1978) have shown that plasma levels give a reasonable estimate of the MIS concentration in a tumour and hence its radiation enhancement ratio. Very few data are available on the distribution of MIS in CSF (Ash *et al.*, 1979). For this reason the level of MIS in CSF was monitored. We have observed concentrations of MIS in CSF in the range of 80–100% of the corresponding plasma levels, showing that MIS passes freely into the CSF via the blood-brain barrier. Recent data from Ash *et al.* (1979) suggest that the maximum CSF level of MIS is obtained four to six hours after application, compared with a maximum level in serum after one to four hours. No study of the pharmacokinetics of MIS in CSF has been conducted to date because of the ethical difficulty in obtaining adequate numbers of samples.

The relationship between MIS administration and irradiation would have obvious direct consequences in optimizing the radiotherapy treatment of gliomas. The data of Ash *et al.* (1979) suggest that irradiation after five to six hours may give the best results. Workman *et al.* (1978b) showed that MIS levels in saliva agreed well with those of the plasma. This method would have obvious advantages in the monitoring of MIS or Ro–05–9963 in patients undergoing therapy, since it is non-invasive and may be particularly suitable for small children and for those patients in whom plasma sampling is unsuitable or impossible. In the present study, salivary MIS and Ro–05–9963 were assayed as an alternative to blood sampling for several patients (data not shown), but with the exception of patient F no correlation between the plasma and salivary levels could be ascertained (Fig. 3).

The metabolism of MIS was found to vary considerably from patient to patient and may be an important factor in the urinary excretion. The amount of MIS and O-demethylated metabolite excreted in 24 h accounts for less than 40% of the dose given. These findings are in agreement with those of Flockhart *et al.* (1978). Similar data have been found in animal experiments (White *et al.*, 1979a). There does seem to be a significant change in the proportion of MIS or Ro–05–9963 excreted in the urine with multiple-dose administration (Fig. 2). Other metabolites have not been identified as yet, largely due to their high solubility in water (Flockhart *et al.*, 1978). We cannot at present explain the high excretion of Ro–05–9963 in the two patients M and K. Drugs known to induce microsomal enzymes such as barbiturates were automatically excluded during therapy. Workman (1979) has shown that MIS induced microsomal enzymes, although its excretion was not affected. It may be that, due to the advanced tumour stage, these patients had an altered metabolism, *e.g.* elevated demethylation, resulting in such a large urinary excretion of Ro–05–9963.

From a radiobiological view it seems that the dosage of MIS in glioma patients (400 mg/m^2) is too low to obtain a measurable therapeutic gain. The phase III study has indicated that the MIS-treated patients show no significant therapeutic gain over placebo-treated patients at the present follow-up stage. According to our preliminary investigations, higher doses of MIS (1 g/m^2)—as in our patients with oesophageal cancer and recurrent brain tumours —are likely to be needed to produce the desired

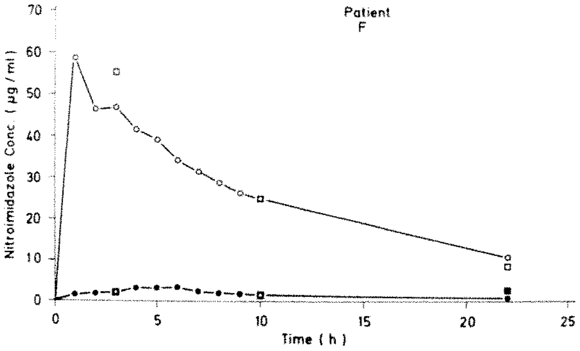


FIG. 3.

The distribution of misonidazole and demethylmisonidazole, Ro–05–9963, in plasma and saliva in a glioma patient after oral administration of misonidazole at 1 g/m^2. ○, ●: Misonidazole and demethylmisonidazole in plasma; □, ■: Corresponding values in saliva.

serum or plasma concentration and radiosensitizing effect in multifractionated schedules.

REFERENCES

Adams, G. E., Fowler, J. F. and Wardman, P., Eds., 1978. Hypoxic cell sensitizers in radiobiology and radiotherapy, (8th L. H. Gray Conference) *British Journal of Cancer*, *37*, Supplement III.

Ash, D. V., Smith, M. R. and Bugden, R. D., 1979. Distribution of misonidazole in human tumours and normal tissues. *British Journal of Cancer*, *39*, 503–509.

Bamberg, M., Tamulevicius, P., Streffer, C. and Scherer, E., 1980. Clinical studies with the radiosensitizer misonidazole. In *Current chemotherapy and infectious disease* (11th International Congress of Chemotherapy and 19th Interscience Conference on Antimicrobial Agents and Chemotherapy, 1979, Boston, Mass., USA) (American Society of Microbiology, Washington, D.C.), pp. 1550–1553.

Dawes, P. J. D. K., Peckham, M. J. and Steel, G. G., 1978. The response of human tumour metastases to radiation and misonidazole. *British Journal of Cancer*, *37*, Supplement III, 290–296.

Denekamp, J. and Fowler, J. F., 1978. Radiosensitisation of solid tumours by nitroimidazoles. *International Journal of Radiation Oncology, Biology and Physics*, *4*, 143–151.

Dische, S., Saunders, M. I., Lee, M. E., Adams, G. E. and Flockhart, I. R., 1977. Clinical testing of the radiosensitizer Ro–07–0582: Experience with multiple doses. *British Journal of Cancer*, *35*, 567–579.

Flockhart. I. R., Large, P., Troup, D., Malcolm, S. L. and Marten, T. R., 1978. Pharmacokinetic and metabolic studies of the hypoxic cell radiosensitizer misonidazole. *Xenobiotica*, *8*, 97–105.

Foster, J. L., Flockhart, I. R., Dische, S., Gray, A., Lenox-Smith, I. and Smithen, C. E., 1975. Serum concentration measurements in man of the radiosensitizer Ro–07–0582: Some preliminary results. *British Journal of Cancer*, *31*, 679–683.

Fowler, J. F., Adams, G. E. and Denekamp, J., 1976. Radiosensitizers of hypoxic cells in solid tumours. *Cancer Treatment Reviews*, *3*, 227–256.

Fowler, J. F., Denekamp, J., Page, A. L., Begg, A. C., Field, S. B. and Butler, K., 1972. Fractionation with X rays and neutrons in mice: response of skin and C_3H mammary tumours. *British Journal of Radiology*, *45*, 237–249.

Johnson, R., Gomer, C., Ambrus, J., Pearce, J. and Boyle, D., 1976. An investigation of the pharmacological and radiosensitizing effects of the 2-nitroimidazole Ro–07–0582 in primates. *British Journal of Radiology*, *49*, 294–295.

Partington, J., Koziol, D., Chapman, D., Rabin, H., Urtasun, R. C., 1979. New side effect of the hypoxic cell sensitizer, misonidazole. *Cancer Treatment Reports*, *63*, 123–125.

Saunders, M. I., Dische, S., Anderson, P. and Flockhart, I. R., 1978. Neurotoxicity of misonidazole and its relationship to dose, half-life and concentration in the serum. *British Journal of Cancer*, *37*, Supplement III, 268–270.

Urtasun, R. C., Band, P. R., Chapman, J. D., Rabin, J. R., Wilson, A. F. and Fryer, C. G., 1977. Clinical phase I study of the hypoxic cell radiosensitizer Ro–07–0582, a 2-nitroimidazole derivative. *Radiology*, *122*, 801–804.

White, R. A. S., Workman, P., Freedman, L. S., Owen, L. N. and Bleehen, N. M., 1979a. The pharmacokinetics of misonidazole in the dog. *European Journal of Cancer*, *15*, 1233–1242.

White, R. A. S., Workman, P., Owen, L. N. and Bleehen, N. M., 1979b. The penetration of misonidazole into spontaneous canine tumours. *British Journal of Cancer*, *40*, 284–294.

Wiltshire, C. R., Workman, P., Watson, J. V. and Bleehen, N. M., 1978. Clinical studies with misonidazole. *British Journal of Cancer*, *37*, Supplement III, 286–289.

Workman, P., 1979. Effects of pretreatment with phenobarbitone and phenytoin on the pharmacokinetics and toxicity of misonidazole in mice. *British Journal of Cancer*, *40*, 335–353.

Workman, P., Little, C. J., Marten, T. R., Flockhart, I. R. and Bleehen, N. M., 1978a. Estimation of the hypoxic cell sensitizer misonidazole and its O-demethylated metabolite in biological material by reversed phase high performance liquid chromatography. *Journal of Chromatography*, *145*, 507–512.

Workman, P., Wiltshire, C. R., Plowman, P. N. and Bleehen, N. M., 1978b. Monitoring salivary misonidazole in man: A possible alternative to plasma monitoring. *British Journal of Cancer*, *38*, 709–718.

Book review

Heavy Particle Radiotherapy. By M. R. Raju, pp. vii+500. 1980. (Academic Press, New York), £20·60/$36.50.
ISBN 0-12-576250-X

This book provides an excellent summary of the state of play with neutrons, protons, helium ions and other nuclei up to argon, and negative pi mesons. The physical and radiobiological properties of all these beams are discussed in considerable detail, together with the clinical results when this is possible. The results presented are remarkably up-to-date, especially valuable in such a quickly developing area, with references up to 1979.

The book is particularly useful for anyone wanting to know the extent of current knowledge on any of these beams. It contains numerous tables listing the radiobiological studies made with each beam and giving the RBE and OER values found and other relevant factors such as dose rate and the volume over which a Bragg peak was spread. The list of references is particularly extensive. It is good to see that as well as very recent ones, references are also given to early work so that the reader is reminded, for example, of the discoveries made by Mottram and Spear in the 1930s about the sensitizing effect of oxygen.

Dr. Raju has himself made notable contributions to the radiobiology of beams of heavy ions and pi mesons used under radiotherapeutic conditions, with the peaks spread to varying extents. But he has not ignored the contributions of others and has succeeded in presenting a well-balanced account.

The book starts with two chapters on radiobiological effects and closes with an appendix on radiobiological techniques. Between are the chapters on the individual types of radiation, in which physics and dosimetry receive at least as much emphasis as the biology.

In appearance the book looks like type reproduced photographically, with no justification of the lines. Nevertheless, the effect is clear and not unpleasing. The diagrams are particularly sharp and easy to read. The binding is excellent and the book stays open at any page.

D. K. Bewley.

1981, *British Journal of Radiology*, *54*, 325–327

APRIL 1981

Indium (^{111}In)-labelled platelets in the diagnosis of renal transplant rejection: preliminary findings

By *A. Fenech, M.D., M.R.C.P., †A. Nicholls, M.B., M.R.C.P. and ‡F. W. Smith, D.M.R.D., F.F.R.

Department of Medicine and ‡Department of Medical Physics, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZD

ABSTRACT

Eleven patients with recent kidney transplants have undergone serial pelvic imaging after autologous platelet labelling with indium-111. Rejection was accompanied by marked platelet deposition in the graft, whereas acute tubular necrosis was characterized by minimal platelet accumulation. The method has been quantified by comparing counts over the graft to counts from a similar area on the opposite site, and appears to distinguish between the two main causes of renal failure after transplantation. In addition, complications of transplant surgery may be demonstrated.

The various causes of renal failure after kidney transplantation may be difficult to define, and differentiation of acute tubular necrosis from rejection is a major problem. Platelets are secondarily involved in both cellular and humoral rejection (Finkelstein *et al.*, 1976); study of radionuclide-labelled platelet accumulation in kidney grafts might therefore provide insight into some of the mechanisms of graft rejection and also prove useful in diagnosis. Accumulation of ^{111}In-labelled platelets has been demonstrated to occur within rejecting renal allografts (Smith *et al.*, 1979), but the diagnostic value of such investigation is not clear. We report here our preliminary experience with ^{111}In-labelled platelets in the post-operative study of patients after cadaver renal transplantation.

PATIENTS AND METHODS

Eleven consecutive patients (eight male, three female) aged 20–50 years were studied during the first fortnight after transplantation. The study was approved by the local ethical committee, and informed consent was obtained from patients. The immunosuppressive therapy and routine investigations have been detailed elsewhere (Whiting *et al.*, 1981). Autologous platelets were labelled with 370–555 kBq (150–200 μCi) ^{111}In-oxine (The Radiochemical Centre, Amersham) by the method of Hawker *et al.* (1980) between the fifth and tenth days postoperatively. The method required only 26 ml venous blood and the highest dose of radiation was to the spleen which received approximately 3–4 cGy (rad). Pelvic imaging for five min with a wide-field gamma camera fitted with a medium energy collimator (Ohio Nuclear 410 S), linked to a Gamma 11 computer system (Digital Equipment Corporation), was performed daily for up to five days after labelling. The distribution of counts within the field of view was noted, and the ratio of the counts over the transplanted kidney to counts from a similar area on the opposite side was obtained (graft: opposite-side ratio). Care was taken to exclude counts from extra renal sites before calculating the graft: opposite side ratio (see below).

RESULTS

Thirty-eight images from ten of the 11 patients were analysed. Patient 2 inadvertently had platelet labelling performed just before dialysis and therefore was not scanned on the assumption that platelets lost on the membrane would render the investigation valueless; subsequent experience with patients 10 and 11 suggested that this assumption was incorrect as useful data was obtained after dialysis. The results of the scans and the status of the patients at the time of imaging are indicated in Table I.

Seven patients (Nos. 1, 3–6, 8 and 11), none of whom showed evidence of rejection at any stage, had a total of 26 scans performed. In all 26 the graft: opposite-side ratio was less than 1.5 and tended to remain constant during the period of observation. A typical scan is shown in Fig. 1. As indicated in the table, these patients had either good graft function or acute tubular necrosis. Patient 7 had classical acute rejection (oliguria, fever, graft enlargement) on day seven. His first scan on day eight showed no platelet uptake by the transplant but subsequent scans on days 9–11 showed striking accumulation of platelets within the kidney (Fig. 2). Patient 9 had graft: opposite-side ratios greater than 1.5 on two days; during this period of scanning there was a transient fall in urine output and rise in serum creatinine. No anti-rejection therapy was given, and subsequently renal function improved but this episode of renal failure was considered to be due to rejection. Patient 10 had severe early rejection, and all his scans showed graft: opposite-side ratios greater than 1.5.

---

*Present address: Department of Cardiology, Glasgow Royal Infirmary, Glasgow G4 0SF.

†Present address: Renal Unit, Royal Hallamshire Hospital, Sheffield S10 2JF.

TABLE I

Graft: opposite-side ratios and clinical status of 11 patients undergoing ^{111}In-platelet scans

Patient No.	Days scanned	Graft: opposite-side ratios	Other features	Clinical status during scans
1	8–10	1.3, 1.3, 1.3	—	ATN in recovery
2	—	—	—	Severe ATN
3	5–8	1.0, 1.0, 1.0, 1.0	—	ATN in recovery
4	6–8	1.2, 1.2, 1.2	—	ATN
5	6–10	1.0, 1.0, 1.0, 1.0, 1.0	—	Good graft function
6	6–10	1.4, 1.4, 1.4, 1.4, 1.4	Peri-renal accumulation of platelets	Good graft function; haematoma
7	8–11	1.1, 3.5, 3.5, 3.5	—	Rejection from day 7
8	8–11	1.0, 1.3, 1.5, 1.5	—	Good graft function
9	5–7	1.5, 1.6, 2.0	Platelet accumulation in pelvic veins	Transient creatinine rise; DVT
10	10–14	1.6, 2.1, 2.0	—	Severe rejection (from day 3)
11	8–9	1.1, 1.1	Peri-renal accumulation of platelets	Severe ATN; haematoma

ATN—acute tubular necrosis; DVT—deep venous thrombosis.

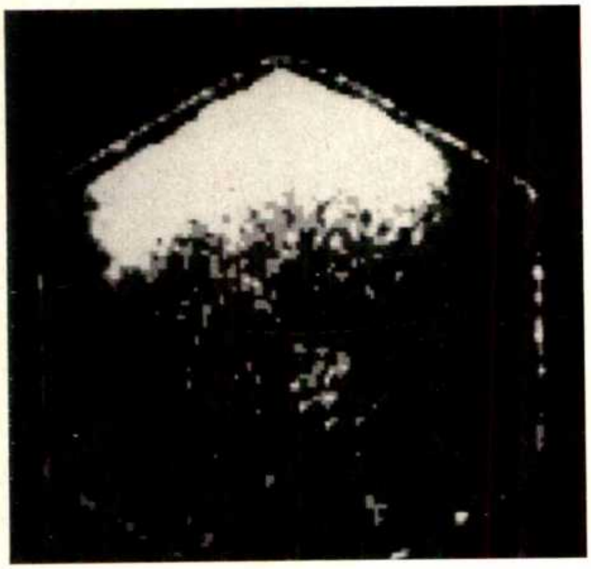


Fig. 1.

Stable, functioning graft situated in the left side of the pelvis. There is minimal uptake of platelets within the kidney (graft: opposite-side ratio 1.2:1).

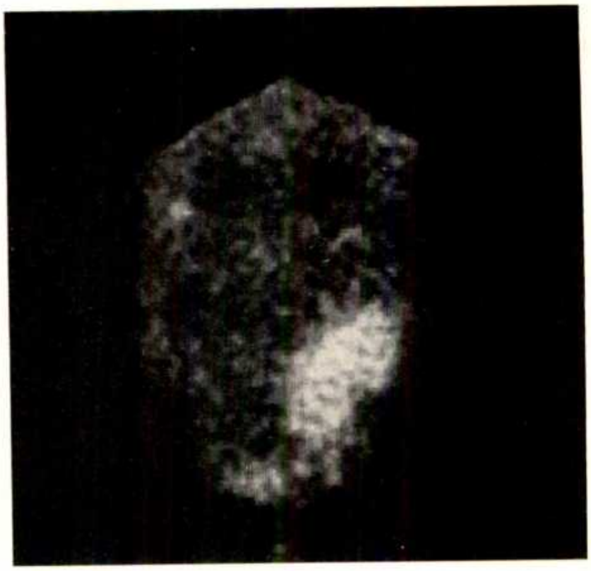


Fig. 2.

Marked accumulation of labelled platelets by an acutely rejecting kidney (graft: opposite-side ratio 3.5:1).

Three patients (Nos. 6, 9, 11) had scans which repeatedly showed *extra* renal accumulation of platelets; this was demonstrated either by external markers, or by simultaneous performance of a ^{99}Tc^{m} pertechnetate scan. As indicated above, these counts from extra-renal sites were excluded from calculation of graft: opposite side ratios. Patient 9 was considered to have a pelvic deep venous thrombosis (Fig. 3) by criteria previously discussed by us (Fenech *et al.*, 1980); DVT was confirmed by venography. Two patients (Nos. 6 and 11) had peri-renal accumulation of platelets suggesting the presence of haematomata. Superimposition of a ^{99}Tc^{m} pertechnetate perfusion scan upon the platelet scan confirmed the extra renal location of platelets in these cases (Fig. 4), and ultra-sound scanning resulted in similar conclusions.

Discussion

These results show accumulation of platelets in renal allografts undergoing episodes of acute rejection. For the calculation of the graft: opposite-side

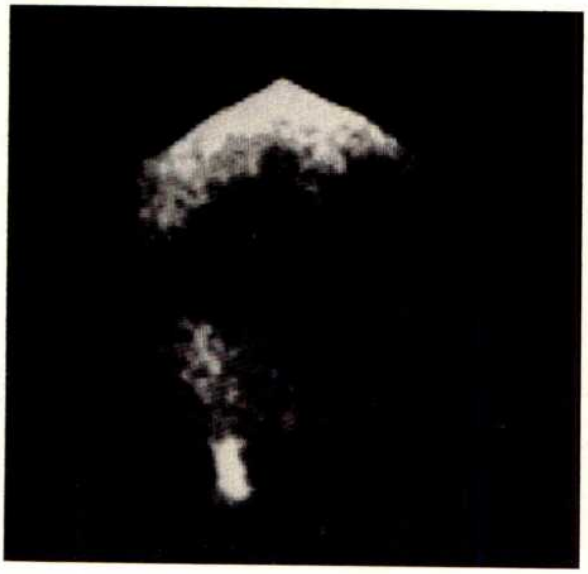


FIG. 3.

Extra-renal accumulation of platelets over the right internal iliac vein; DVT confirmed by venography.

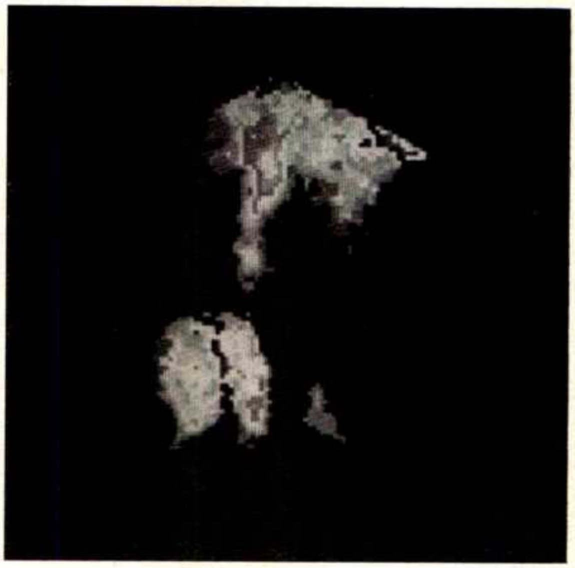


FIG. 4.

Composite image of $^{99}Tc^{m}$ pertechnetate renal perfusion scan and ^{111}In platelet scan. The accumulation of platelets is extra-renal, and probably represents a haematoma.

ratio, data quantification must exclude counts from extra renal sites. With this proviso, we have found a ratio less than 1.5 to occur in patients with good graft function or undergoing episodes of acute tubular necrosis. Ratios of greater than 1.5 have occurred only during episodes of rejection. We do not yet know whether abnormal platelet accumulation necessarily occurs early during rejection, so the predictive clinical value of the test is not yet defined; scans initiated earlier in the post-operative phase may provide this information.

A possible disadvantage of this method arises in those patients needing dialysis after transplantation. Theoretically, platelet loss on dialysis membranes may limit the period after labelling during which useful data are obtainable by this method. However, patients 10 and 11 were dialysed between first and subsequent scans, the ratios remaining unchanged though the absolute counts diminished. This suggests that dialysis may not prevent the acquisition of useful information from the technique. We are currently evaluating the use of more frequent platelet labelling with a lower dose of ^{111}In, and longer imaging time, which may minimize this problem.

In summary, serial pelvic imaging after ^{111}In-oxine-labelling of autologous platelets appears a promising method for elucidation of the cause of episodes of renal failure after kidney transplantation. Provided extra-renal platelet accumulations are excluded from calculations, abnormal ratios appear to occur only during episodes of rejection, whereas in acute tubular necrosis, repeatedly normal ratios have been found. Our data do not indicate whether platelet deposition in rejecting kidneys is observed before or after rejection is established and has been detected by other criteria. With further refinement the method may, however, provide a useful additional aid to the diagnosis of rejection; it also provides valuable information about some of the extra-renal complications of renal transplant surgery.

ACKNOWLEDGMENTS

We thank Dr. G. R. D. Catto, Dr. N. Edward, and Mr. J. Engeset for permission to study patients under their care, and Dr. B. Bennett and Professor A. S. Douglas for helpful advice.

REFERENCES

FENECH, A., DENDY, P. P., HUSSEY, J. K., BENNETT, B. and DOUGLAS, A. S., 1980. Indium-111 labelled platelets in diagnosis of leg-vein thrombosis: preliminary findings. *British Medical Journal*, *ii*, 1571–1573.

FINKELSTEIN, F. O., SIEGEL, N. J., BASTL, C., FORREST, J. N. and KASHGARIAN, M., 1976. Kidney transplant biopsies in the diagnosis and management of acute rejection reactions. *Kidney International*, *10*, 171–178.

HAWKER, R. J., HAWKER, L. M. and WILKINSON, A. R., 1980. Indium (^{111}In)-labelled human platelets: optimal method. *Clinical Science*, *58*, 243–248.

SMITH, N., CHANDLER, S., HAWKER, R. J., HAWKER, L. M. and BARNES, A. D., 1979. Indium labelled autologous platelets as diagnostic aid after renal transplantation. *Lancet*, *ii*, 1241–1242.

WHITING, P. M., NICHOLLS, A. J., CATTO, G. R. D., EDWARD, N. and ENGESET, J., 1981. Patterns of N-acetyl-β-D-glucosaminidase (NAG) excretion after transplantation. *Clinica Chimica Acta* (in press).

1981, *British Journal of Radiology*, 54, 328–334

Portable transfer digital dosemeter for beam output measurements with X and gamma rays, electrons and neutrons

By A. Sankaran, M.A., B.Sc., R. S. Gokarn, B.Sc., D.R.E. and P. Gangadharan, M.A., M.S.

Division of Radiological Protection, Bhabha Atomic Research Centre, Trombay, Bombay-400 085, India

(Received November 1979 and in revised form November 1980)

ABSTRACT

This instrument was developed in response to a requirement for an accurate, stable and portable transfer dosemeter for calibration, at therapy dose levels, of equipment used for generating X and γ rays, electrons and neutrons. The detector is a 0.5 cm^3 ionization chamber capable of fitting various wall materials reproducibly at the end of the chamber stem. The measuring system uniquely combines the features of a MOSFET electrometer and an automatic Townsend balance. When used for X, γ and neutron radiations, the instrument measures the tissue kerma in free air on two ranges: 0.001–1.999 Gy (0.1–199.9 rad) and 0.01–19.99 Gy (1–1999 rad) or their exposure equivalents, with autoranging feature when the first range is exceeded. The polarizing voltage (180 V) can be reversed for electron and neutron dosimetry.

The dosemeter has a measuring accuracy of $\pm 0.2\%$ FS ± 1 digit and operates on four 1.5 V torchlight cells or on AC mains (200–250 V, 50–60 Hz). It utilizes solid state devices, CMOS integrated circuits and displays, and is not affected by RF fields. The instrument is enclosed in a briefcase for portability and is easy to operate and maintain in a hospital.

Radiation therapy requires accurate dosimetry for effective treatment and for comparison of treatment methods and biological and clinical results from various institutions (Lanzl, 1978; Herring and Compton, 1970). For achieving these objectives, there is a need for a dosemeter which is accurate, stable and reliable and which, in addition, is portable and easy to operate and maintain so that it can be used as a transfer instrument. Recently, the advantage of fast neutrons for radiobiological and medical applications has given rise to the proliferation of various types of neutron equipment which has, in turn, necessitated instruments for calibration of these generators. Many sophisticated instruments are commercially available for X and γ ray dosimetry but at present there is perhaps no single instrument for use with various radiations. For dosimetry intercomparison between fast neutron facilities, the need for a transfer dosemeter has been particularly felt (Greene and Miles, 1976; Smith *et al.*, 1975; IAEA, 1978). The instrument described in this paper was developed to meet these requirements. It was primarily developed for beam output measurements with X and γ rays and electrons but can be extended for calibration of neutron generators as well.

DESIGN OF INSTRUMENT

Chamber

The detector is a 0.5 cm^3 ionization chamber at the end of a 105 mm aluminium stem. Figure 1 shows the schematic drawing of the ionization chamber assembly. The stability and reproducibility of the air volume are ensured by screwing and tightening the outer aluminium stem. The chamber is fully vented to atmosphere. Thimbles fabricated out of various wall materials, viz., pure graphite (reactor grade), Tufnol, polystyrene, tissue equivalent (TE) plastic (made out of Shonka A-150 plastic) and Teflon are provided for the measurement of various radiations. The chamber assembly is so designed that the thimbles, which are carefully machined to be of identical size, can be interchanged without any appreciable change in air volume. Suitable build-up caps of various materials, having requisite wall thickness for measuring high-energy γ and neutron radiations, have been provided. As can be seen from Fig. 1, the chamber is fully guarded which eliminates radiation-induced conductivity in the stem insulator. Also, any of the commonly available insulators can be used for the central conductor (*e.g.* polystyrene). Full guarding of the stem is ensured by coating the entire outer surface of the insulator surrounding the central conductor with colloidal graphite, taking care to see that the coating does not extend into the sensitive volume of the chamber, as this would distort the electric field inside the chamber. The effect of the guard on the electric field inside the chamber was checked by comparing its sensitivity with an identical unguarded chamber for hard X rays over a range of exposure rates from 0.1–10 Gy/min air kerma (10–1000 R/min), due correction being applied for the stem leakage, etc. of the latter. The difference in response between the chambers was less than 1%. Guarding the stem brought the following additional advantages: (i) the stem of the chamber does not require any prior irradiation to stabilize the insulator characteristics, (ii) the chamber insulator surface leakage under conditions of high ambient humidity (encountered in tropical regions of the world) is

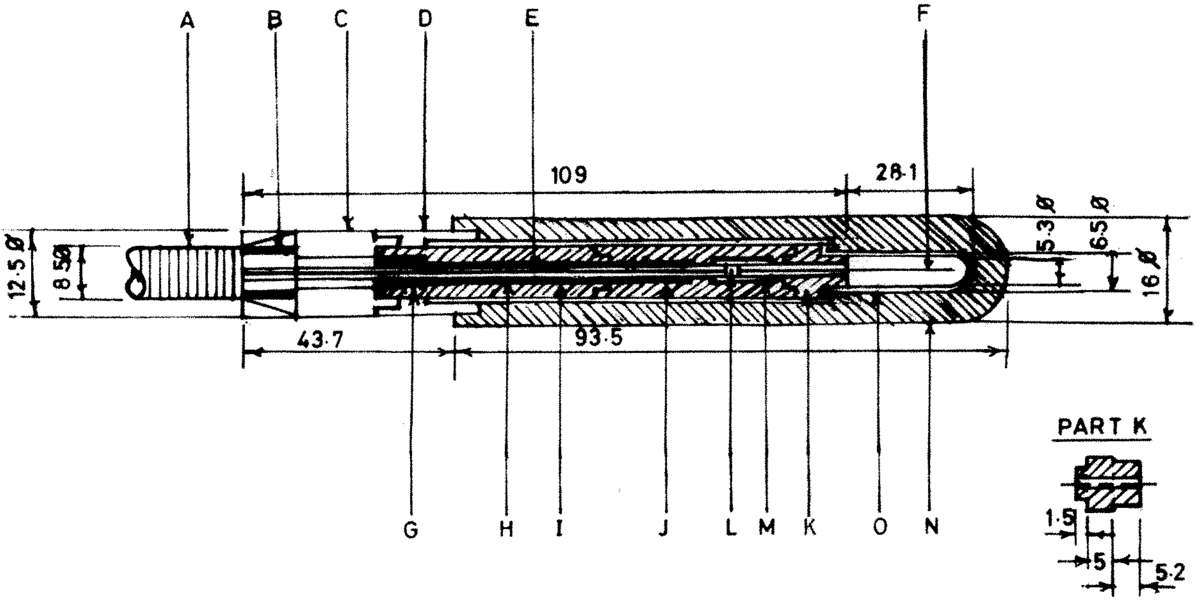


FIG. 1.

Schematic diagram of 0.5 cm^3 ion chamber assembly. A, Cable outer sheath; B, outer braid of cable; C, aluminium; D, aluminium; E, inner conductor of cable; F, inner electrode (pure aluminium); G, inner braid; H, polythene (graphite-coated outside); I, J, K, polystyrene (graphite-coated inside); L, copper-aluminium joint; M, sleeve (Teflon); N, Perspex or TE plastic; O, chamber (Tufnol, polystyrene, graphite, TE plastic or Teflon).

drastically reduced and (iii) a higher polarizing voltage (300 V) can be applied, necessary to achieve near-saturation conditions when the chamber is exposed to pulsed beams (HPA, 1971).

Description of circuit

The chamber is permanently connected to the measuring part by an 8 m long low-noise coaxial cable. The measuring part uniquely combines the features of a MOSFET electrometer and an automatic Townsend balance system with digital display and is based on the continuous-balance type analog-to-digital (A/D) converter. A schematic block diagram of the circuit is shown in Fig. 2. The current from the chamber is integrated by one or both of the capacitors (C_1, C_2) which form the input of a MOSFET feedback amplifier, connected for a closed loop gain of 40. The amplifier employs a dual *p*-channel enhancement transistor (MEM 955, General Instruments, USA), operated as source followers, connected to a micropower operational amplifier (LH 24250). The input gate of the MOSFET has been protected against transient high voltages (*e.g.* shorting of chamber voltage to anode wire) by connecting two ultra-low leakage diodes (Intersil dual diode ID 100) back-to-back in series from input to ground. This combination provides the required input insulation ($> 10^{15}$ Ω) at voltages up to 10 V and begins to break down at higher input voltages (positive or negative), thereby protecting the MOSFET from damage.

The output of the amplifier is sensed by two comparators one and two (upper and lower) having their reference voltages at +100 mV and −100 mV respectively. The output of one of the comparators gates a ten kHz oscillator to an up-down binary counter (three stages of scale-of-16 counter 74 C 193). The 12-bit outputs of the binary counter are connected to a digital-to-analog converter, (DAC) utilizing a commercially available low-power inexpensive IC chip (Analog Devices, AD 7531J), operated in the bipolar mode. The output currents of the DAC (I_1 and I_2) are summed by two operational amplifiers (LH 24250). For bipolar operation, the DAC is initially reset to zero with the most significant bit at "1" state and the other bits at "0" state. Depending on the output state of the upper and lower comparators, the counters count "up" or "down" and the DAC swings positive or negative up to V_{ref} (reference voltage applied to the DAC $\approx$10 V). The output of the DAC is connected to the bottom end of the input capacitors (C_1 or C_2) which constitutes an automatic Townsend balance. The automatic balance obviates the need for another null meter and also means that balancing during or after exposure, which is necessary in other dosemeters, is completely dispensed with. The pulses fed to the binary counters are also counted by the four stage up-down decade counters (74 C 192) which are strobed and displayed on a 3½-digit LED; or, alternatively, without strobing on an LCD display.

All the regulated voltages required for the circuits (+15 V, −15 V and +10 V) and chamber (±180 V) are obtained from a DC–DC converter. The switch SW3 has been provided to interchange simultaneously the up-down inputs of the decade counter when the polarity of the chamber voltage is reversed. The presence of chamber voltage is indicated by a panel neon display which forms part of the neon regulators for ±180 V supply. The instrument measures doses up to 1.999 Gy (199.9 rad) with capacitor C_1 (3668 pF, 3600 pF in parallel with 68 pF). When the output of the DAC exceeds ±10 V, one of the comparators (three or four) is triggered, closing the reed switch (SW2) and putting the capacitor C_2 (33000 pF) in parallel with C_1, thereby bringing down the sensitivity by a factor of exactly ten. (Capacitors C_1 and C_2 should preferably have been 3000 pF and 27000 pF since they are standard values but could not be used because of the output swing limitations of the DAC used: (±10 V)). With this arrangement, the full range becomes 19.99 Gy (1999 rad) which is indicated by the change of decimal point on the display.

A precision timer (NE 555) with a repeatability of better than ±0.5% has been provided for accurately timing the exposure for routine measurements. Timing intervals of 30, 60, 120 seconds and "∞" have been provided. Reed switch SW1 in combination with SW2 (both Hamlin type MRH-15) accomplishes the charge integration over a wide range (1 mGy–20 Gy). Special care has been taken in the design of the reed relay assembly to reduce the production of stray charges at the input caused by opening and closing of the reed switch contacts. To achieve this, the reed switch contacts and the relay coils have been surrounded by grounded copper foils. The same reed switch SW1 performs the functions of

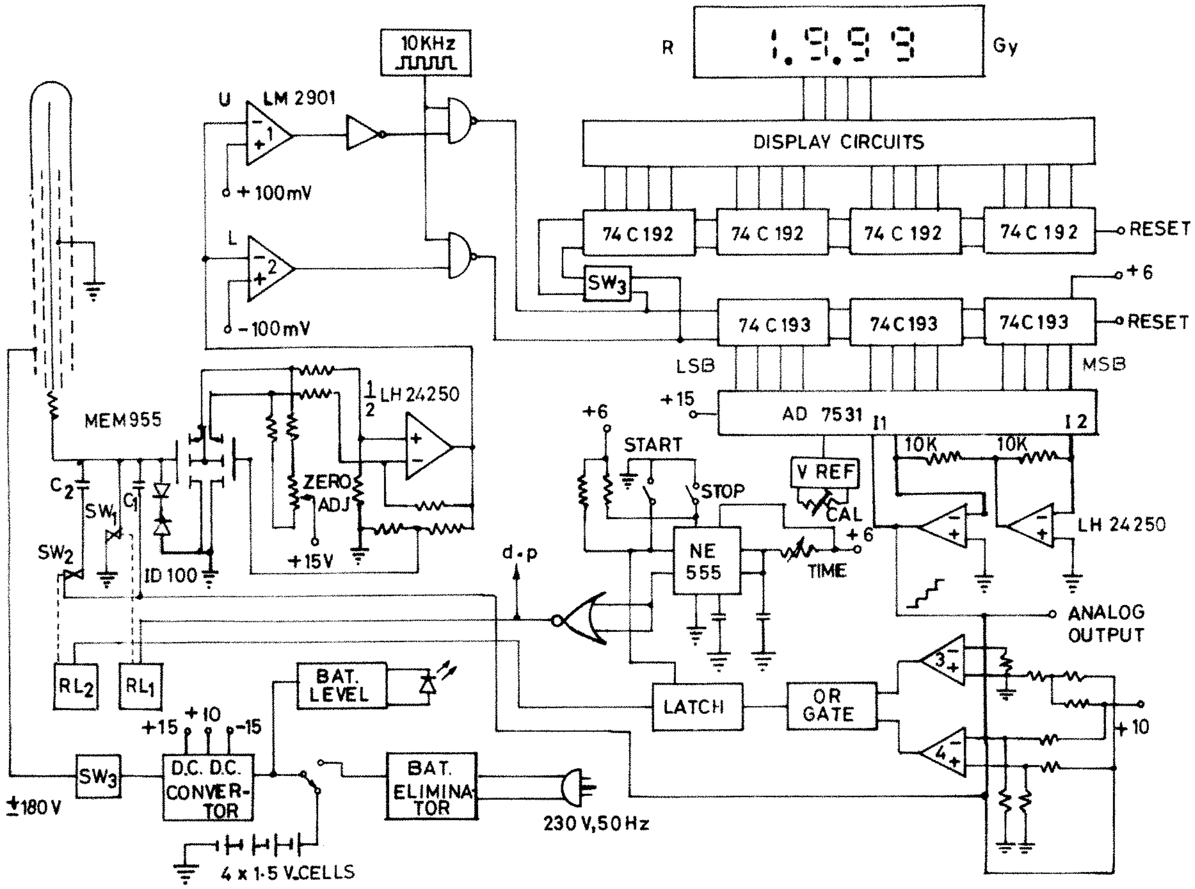


Fig. 2.
Schematic block diagram of the circuit of the dosemeter.

initiation and termination of integration. The timer opens the contacts of the switch SW1 across capacitor C_1 when the "start" button is depressed and resets the capacitor at the end of the timing interval or when the exposure is interrupted by depressing the "stop" button during a set timing interval. A third "reset" button has been provided to reset the DAC and the counters. When, however, this feature is a disadvantage and it becomes necessary to integrate a number of successive exposures, the timer switch can be kept at the ∞ position and the radiation equipment may be switched on and off, the timing being done by the built-in timer in the generator. In this mode, there is an added advantage that the dose reading after an exposure can be repeated by recycling any number of times by pressing and releasing the "reset" button. This resets the DAC and the display but not the input capacitor, resulting in the correct display of voltage across the input capacitor, thereby avoiding any error in the display due to spurious pulses which would have occurred during exposure. The use of up-down counters with a bipolar DAC enables not only measurement of positive as well as negative ionization currents but also facilitates detection of leakage currents in the electrometer and input capacitor. In addition, the "zero adj" control (voltage offset) provided for the input amplifier can be used to check the overall operation of the system, *e.g.* comparator states, oscillator frequency and up-down counter operation.

A removable Perspex silica-gel container serves to keep the components inside the box dry and detects presence of excess ambient humidity. The autoranging feature obviates the necessity of using a high-resistance switch to select C_1 or C_2 and thereby facilitates sealing (though not hermetic) of the input box against external contaminants and humidity. The input leakage current present under adverse climatic conditions can be revealed by allowing the capacitor C_1 to integrate exposures such that the voltage across capacitor C_1 is maximum (≈ 10 V) and subsequently recycling after keeping the "reset" button depressed for a sufficiently long time (say, one minute) and releasing it, as described earlier. In the depressed position, the DAC is reset to zero and consequently the capacitor voltage appears across the input insulation. If the readings decrease progressively after each recycling, leakage current caused by lowering of input insulation is present. In this case, the silica gel crystals may be rejuvenated and/or the elements inside the input box dried.

USE FOR VARIOUS RADIATIONS

X and gamma-ray dosimetry

The reproducibility of the air volume with various thimbles was checked indirectly by measuring their response to ^{60}Co radiation. For this purpose, each chamber was fitted with a build-up cap of Perspex. Table I shows the relative sensitivity of the chambers (Tufnol = 1.00) which is seen to be within $\pm 4\%$. This includes the sensitivity variation due to the mass-energy absorption coefficients and stopping-power ratios (actually the quotient, $\mu_{en}/\rho S_g^m$) of various wall materials used for the chamber. Table I also shows the quality dependence of the chamber with various wall materials and a 1 mm diameter pure aluminium wire. The details of calibration qualities used are mentioned elsewhere (Sankaran

TABLE I

X- AND GAMMA-RAY ENERGY DEPENDENCE AND RELATIVE RESPONSE OF THE 0.5 CM^3§ CHAMBER WITH VARIOUS WALL MATERIALS

Effective energy, keV‡	Correction factor					
	Tufnol*	Polystyrene*	Teflon*	TE plastic*	Graphite*	Graphite†
29	1.01	1.01	0.80	0.85	1.12	1.02
37	1.00	1.01	0.77	0.84	1.10	1.00
55	1.00	1.02	0.81	0.89	1.08	1.02
79	0.99	1.00	0.86	0.93	1.02	1.01
120	0.99	1.01	0.94	0.96	1.01	0.98
129	1.01	1.00	1.04	1.00	1.00	1.00
1250	1.00	1.00	1.00	1.00	1.00	1.00
Relative sensitivity at 1250 keV (Tufnol = 1)	1.00	1.04	0.96	1.04	1.01	1.02

*1 mm diameter pure Al anode wire.
†1 mm diameter pure Al anode wire with Al sleeve.
‡For details of X-ray qualities used, see Sankaran and Gangadharan (1980).
§Actual volume of chamber varies from 0.49 to 0.53 cm^3 between various batches.

and Gangadharan, 1980). For the energy range 29–129 keV, lightly filtered X rays from an X-ray generator were used. A ^{60}Co unit has been used for the highest energy (1250 keV). The comparison standards were reference chambers calibrated against free-air and graphite-cavity ionization chambers maintained in this Division. The readings have been normalized for ^{60}Co (1.00). Table I shows that polystyrene and Tufnol walls give a quality dependence within 2% for X and γ rays in the energy range 30 keV–1.25 MeV. Since the atomic number of graphite is less than the effective $\bar{Z}$ of Tufnol (laminated plastic made of phenol formaldehyde urea in paper) and polystyrene, a lower response at lower energies is exhibited by the graphite chamber. The effect of adding an aluminium sleeve (made of high purity aluminium foil) over the 1 mm anode wire is also given in the Table which shows the improvement obtained. Similar results have been reported earlier (Aird and Farmer, 1972; Kemp, 1972). TE plastic and Teflon chambers have poorer energy response characteristics in view of their higher effective atomic numbers, but for the γ energy range encountered in mixed *n*, γ fields (200 keV–2 MeV) this is quite adequate. The dosemeter is normally calibrated to read exposure in röntgens but can be recalibrated, if necessary, to read directly the tissue kerma in air in Gy (NPL, 1974; HPA, 1969; SCRAD, 1971). Calibration for a particular chamber can be adjusted with the potentiometer (CAL) which varies the reference voltage supplied to the DAC (Fig. 2).

Electron dosimetry

The 0.5 cm^3 polystyrene chamber is recommended for this application in the energy range 5–50 MeV. The output of the generator is calibrated by using this chamber inside a polystyrene phantom (HPA, 1971; SCRAD, 1966). Two readings with the chamber voltage polarities reversed may be obtained by using the switch SW3.

Neutron dosimetry

A dual chamber system comprising a TE chamber with air cavity for measurement of total dose and a Teflon or graphite chamber with air cavity for the γ component have been proposed for output measurements on cyclotrons and 14.7 MeV (D, T) generators (Bewley and Parnell, 1969; Bewley *et al.*, 1972; Lawson and Porter, 1974). For the same charge collected in a TE chamber exposed separately to γ and pure neutron beams, the tissue kerma due to neutrons (D_t) equivalent to a γ exposure X_c (röntgens) is given by

$$D_t = \frac{\overline{W}_N}{\overline{W}_c} \cdot \frac{(S_{m,\,g})_N}{(S_{m,\,g})_c} \frac{K_t}{K_m} \frac{(\mu_{en}/\rho)_m}{(\mu_{en}/\rho)_{H_2O}} C_\lambda X_c$$

where the symbols have their usual meanings (Williams *et al.*, 1979). For typical neutron beams in the energy range 7–21 MeV, this gives (Smith *et al.*, 1975; SCRAD, 1971);

$$D_t \approx 0.98\ X_c \text{ to } 1.01\ X_c.$$

This shows that if the instrument is calibrated for ^{60}Co radiation with a TE chamber (with air cavity) to read exposure in röntgens, it can be used to measure directly the neutron dose (tissue kerma in free air in rad) or to measure the total dose (n+γ) when the chamber is exposed to a mixed n, γ beam containing a small γ component.

The performance of the instrument in this mode, however, could not be experimentally substantiated due to the non-availability of high-intensity fast neutron beams and neutron primary dose standards in this centre. It is proposed to confirm these findings experimentally and report at a future date.

RESULTS AND DISCUSSION

The input leakage current of the dosemeter is extremely small ($< 10^{-15}$ A), confirmed by leaving the instrument on (with the "start" button depressed) in the usual measurement mode, with the timer switch set at ∞. The leakage of the instrument over a period of eight hours was not detectable on the display, *i.e.* it was not more than 000.1 R on display. The linearity of the dosemeter for positive and negative currents has been checked with the 0.5 cm^3 chamber in a ^{90}Sr check source and noting the response with various timing intervals (Fig. 3). The linearity is seen to be within $\pm 0.2\%$ FS ± 1 digit, which can be improved to $\pm 0.05\%$ FS ± 1 digit by using the more expensive version of the DAC (AD 7531L). The input voltage required for change of state of either of the comparators is less than about 5 mV, the bit resolution of the DAC in the bipolar mode. For X and γ radiations in the energy range 30 keV–1.3 MeV, an overall accuracy of $\pm 3\%$ in dose measurement can be obtained with the instrument. For other radiations, the accuracy is limited by the various factors which enter into the dosimetric calculations and an overall accuracy of better than $\pm 10\%$ (IAEA, 1978; ICRU, 1977) can be realized. The dosemeter operates on four 1.5 V torchlight cells (Eveready Type 1050 or equivalent). The measuring accuracy is not affected until the battery voltage falls below 5V. A panel LED indicator glows when the voltage falls below this level. A battery eliminator is provided in the instrument. When it is

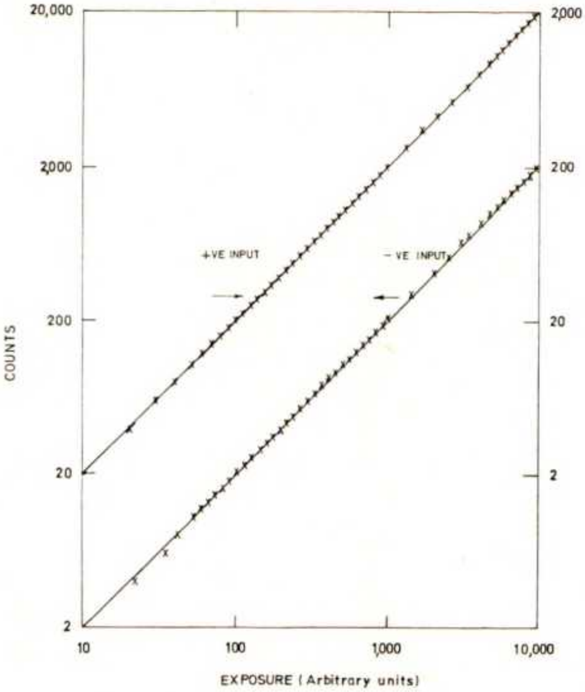


FIG. 3.

Linearity of the dosemeter for positive and negative currents.

connected to mains (200–250 V, 50–60 Hz), the batteries are automatically disconnected. When extreme precision and long-term stability are required, the instrument should be operated on mains. Figure 4 is a photograph of the instrument with the detector and the check source. The use of CMOS integrated circuits and LCD display results in minimum battery drain (< 200 mW). For use of the instrument under subdued lighting conditions, the LED display is preferable since LCDs require ambient light for illumination. The use of LEDs increases battery power dissipation somewhat (350 mW) but this is still within the capacity of the batteries used.

CONCLUSION

The dosemeter with its various detectors and other features is ideally suited as a transfer secondary standard for calibration of X-ray and telegamma units, linear accelerators and betatrons. Unlike electrometer valves, the MOSFET used in the instrument is not damaged by RF fields. It can also be employed with appropriate corrections to calibrate therapy neutron facilities; cyclotrons and 14.7 MeV (D, T) generators. The dosemeter is enclosed in a briefcase for easy portability. The long-term reproducibility of calibration, measured with a ^{90}Sr check source, has been found to be better than ±0.5% during the past year under laboratory conditions (20–30°C; relative humidity up to 70%).

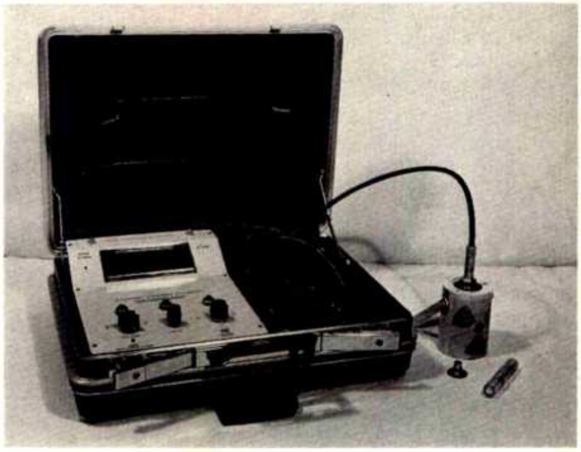


FIG. 4.

Photograph of the instrument with the chamber inside the check source.

ACKNOWLEDGMENTS

The authors thank Dr. K. G. Vohra, Head, Division of Radiological Protection, for constant encouragement and inspiration and the members of the engineering group of this division for fabricating the instrument. Thanks are also due to Mr. M. R. Deokar for his assistance in the design of the instrument.

REFERENCES

AIRD, E. G. A. and FARMER, F. T., 1972. The design of a thimble chamber for the Farmer Dosemeter. *Physics in Medicine and Biology*, *17*, 169–174.

BEWLEY, D. K., MCCULLOUGH, E. C., PAGE, B. C. and SAKATA, S., 1972. Determination of absorbed dose in a fast neutron beam by ionization and calorimetric methods. *Proceedings, First Symposium on Neutron Dosimetry in Biology and Medicine, Germany*, pp. 159–176.

BEWLEY, D. K. and PARNELL, C. J., 1969. The fast neutron beams from the MRC cyclotron. *British Journal of Radiology*, *42*, 281–288.

GREENE, B. and MILES, J., 1976. A transfer instrument for neutron dosimetry. *International Journal of Applied Radiation and Isotopes*, *27*, 239–255.

HERRING, B. F. and COMPTON, D. J. M., 1970. The degree of precision required in radiation dose delivered in cancer therapy. In *Proceedings of the Third International Conference on Computers in Radiotherapy. British Journal of Radiology Special Report 5*, p. 51.

HOSPITAL PHYSICISTS ASSOCIATION, 1969. A code of practice for the dosimetry of 2–35 MV X-ray and Caesium-137 and Cobalt-60 gamma ray beams. *Physics in Medicine and Biology*, *14*, 1–8.

HOSPITAL PHYSICISTS ASSOCIATION, 1971. A Practical Guide for Electron Dosimetry (5–35 MeV). *HPA Report Series 4* (HPA, London).

INTERNATIONAL ATOMIC ENERGY AGENCY, 1978. National and International Standardisation of Radiation Dosimetry. Proceedings of a Symposium, Atlanta, December 1977. Vols. I and II, (IAEA, Vienna).

INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS, 1977. Neutron dosimetry for biology and medicine. *ICRU Report 26*, (ICRU, Washington, DC).

KEMP, L. A. W., 1972. The National Physical Laboratory secondary standard therapy level X-ray exposure meter. *British Journal of Radiology*, *45*, 775–778.

LANZL, L. H., 1978. Why is high accuracy needed in dosimetry? In *Intercomparison procedures in the dosimetry of photon radiation*, IAEA, Technical Report Series No. 182, (IAEA, Vienna).

LAWSON, R. C. and PORTER, D., 1974. Second report on the performance of the Belvidere Hiletron. Report NTP/58, Department of Clinical Physics and Bio-engineering, Belvidere Hospital, Glasgow.

NATIONAL PHYSICAL LABORATORY, HOSPITAL PHYSICISTS' ASSOCIATION and DEPARTMENT OF HEALTH AND SOCIAL SECURITY WORKING PARTY, 1974. The use of a secondary standard to calibrate a field instrument for use in output measurements. *National Physical Laboratory Report RS 3*. (NPL, Teddington).

SANKARAN, A. and GANGADHARAN, P., 1980. Portable versatile X and gamma ray dosimeter for medical use. *Physics in Medicine and Biology*, *25*, 533–541.

SUB-COMMITTEE ON RADIATION DOSIMETRY (SCRAD) OF THE AAPM, 1966. Protocol for the dosimetry of high energy electrons. *Physics in Medicine and Biology*, *11*, 505–520.

1971. Protocol for the dosimetry of X and gamma ray beams with maximum energies between 0.6 and 50 MeV. *Physics in Medicine and Biology*, *16*, 379–396.

SMITH, A. R., ALMOND, P. R., SMATHERS, J. B., OTTE, V. A., ATTIX, F. H., THEUS, R. B., WOOTTON, P., BICHSEL, H., EENMAA, J., WILLIAMS, D., BEWLEY, D. K. and PARNELL, C. J., 1975. Dosimetry intercomparisons between fast neutron therapy facilities. *Medical Physics*, *2*, 195–200.

SUB-COMMITTEE ON RADIATION DOSIMETRY (SCRAD) of the AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE, 1966. Protocol for the dosimetry of high energy electrons. *Physics in Medicine and Biology*, *11*, 505–520.

WILLIAMS, J. R., BONNETT, D. E. and PARNELL, C. J., 1979. The fixed horizontal neutron therapy beam at Edinburgh. *British Journal of Radiology*, *52*, 197–208.

Book reviews

Noncoherent Optical Processing. By G. L. Rogers, pp. xiii+176, 1977 (John Wiley & Sons Ltd., Chichester/New York), £12·65.

This volume in the Wiley Series in Pure and Applied Optics gathers together the essential background theory and outlines many of the practical applications of techniques for processing signals derived from non-coherent optical sources. Hitherto such techniques have been treated on an individual basis; the author makes a refreshing contribution in analysing their features in a systematic manner and explaining their relationships to the more familiar coherent methods.

Non-coherent optical processing consists of methods designed to assist the eye in interpreting input data from ordinary sources of light, which are often of finite size, diffuse and characterized by a wide range of wavelengths. In comparison with coherent systems, the information is passed through many parallel channels and this redundancy results in a greater insensitivity to noise. Alternatively the redundancy may be sacrificed to allow parallel processing of the information, *i.e.* simultaneous performance of various operations.

With suitable positioning of transparent masks and lenses which comprise the optical components, image correlations, convolutions and Fourier transformations are possible. However, since the information is conveyed as a luminance function, a difficulty arises in the handling of negative quantities. The use of the optical equivalent of a DC bias often seriously limits the contrasts attainable in the processed image. A more powerful approach utilizes a spatial or temporal modulation of the source and the text reviews the wide variety of methods recently available, including electronic methods for processing signals derived from optical systems.

Medical applications reviewed in some detail include the use of coded X-ray sources in diagnostic radiology and the use of zone plates and dot coded apertures in nuclear medicine. Neither have led to useful routine procedures and it is clear that in medical images the information is insufficiently "dilute". For example, the result of a comparison of zone-plate and pinhole imaging with a gamma camera is quoted in which the zone-plate methods can only become superior when the proportion of information-containing sites in the image is less than 5% of the total.

In parts the book is so condensed as to be almost incomprehensible without reference to the quoted texts, but in general it is well written and clearly presented. The pages of the book are good examples of non-coherent sources, but while the reader may sometimes require assistance in the interpretation of the data printed thereon, he is unlikely to be aware of redundancy in the information conveyed, and will find the text a coherent source of information on the subject. It will be particularly valuable to those about to embark on practical work in the field.

M. F. COTTRALL.

Radiant Energy and the Eye. By S. Lerman. 1980. pp. ix+321. (Macmillan, New York; Bailliere Tindall, London). £25·00.
ISBN 0-02-369970-1

Professor Lerman and his associates have produced a comprehensive work on radiation and the eye, which with 320 pages is short enough to be readable. The effects of all forms of radiant energy, ultraviolet, visible, infrared, microwave and ionizing radiation are discussed. The basic biological effects are described together with the special effects upon the eye. For those readers unfamiliar with the anatomy and physiology of the eye there is a good section to deal with these.

For the radiotherapist, primarily concerned with the effects of ionizing radiation upon the eye, the amount of information is necessarily limited by the comprehensive scope of this book, but a useful selection of references is given. This book is particularly useful to those concerned with the medicolegal aspects of presumed radiation damage to the eye and to those concerned with radiation protection.

N. P. BROWN.

1981, *British Journal of Radiology*, *54*, 335–338 APRIL 1981

Ultrasound appearances of liver hydatid disease

By E. A. Niron, M.D. and H. Özer, M.D.

Department of Radiology, Aegean University, Faculty of Medicine, Izmir, Turkey

(*Received June 1980 and in revised form September 1980*)

ABSTRACT

The grey scale ultrasound features of liver hydatid disease have been evaluated on 65 surgically proven cysts in 38 patients. The majority of cysts showed the well-known ultrasound pattern of simple cysts. However, a minority of lesions were either multicystic or gave the appearance of a cyst within a cyst. Occasionally cysts showed a feature which we have called "the ultrasonographic water lily sign". Hydatid sand was also occasionally seen in the most dependent portion of hydatid cysts. We have noted that if a hydatid cyst becomes secondarily infected these typical ultrasound patterns are lost and the ultrasound diagnosis may then become more difficult.

In those parts of the world where echinococcal cysts are endemic they comprise the large majority of liver masses presenting for evaluation. There have been relatively few reports in the English literature of the grey scale ultrasound appearances of liver hydatid disease (Taylor *et al.*, 1976; Garrett *et al.*, 1976; Babcock *et al.*, 1978; Alltree, 1979). Although these reports describe the more typical ultrasound features of hydatid disease none has described the full range of appearances which may be produced by this condition.

In this paper we present our experience with a grey scale ultrasound evaluation and pathological correlation of liver hydatid disease in 38 surgically proven cases.

SUBJECTS AND METHOD

Thirty-eight patients were included in this trial, 20 male and 18 female. The patients' ages ranged from 12 to 70 years. A total of 65 hydatid cysts were surgically removed and varied in size from 3 to 20 cm. The majority of cysts were located within the right lobe of the liver.

Ultrasound examinations were performed with a commercially available grey scale B-scanner (Picker Echoview, EDC). A 2.25 MHz, 19 mm long focus transducer was used and scans were generally performed at 1 cm intervals across the entire abdomen in both longitudinal and transverse planes.

RESULTS

We have divided the ultrasound features into three groups. The first group consisted of cysts demonstrating the most commonly seen features; more or less a spherical shape, clearly defined outline, unilocular and completely anechoic (Fig. 1). When these cysts were punctured during surgery clear fluid was aspirated. Forty of our 65 cysts demonstrated this ultrasound pattern.

Group 2 is composed of those cysts showing the less common features of hydatid disease. These are (a) multicystic appearance or "cyst within a cyst" (Fig. 2A, B), (b) detached or collapsed germinal layer, "the ultrasonographic water lily sign" (Fig. 3A, B) (c) evidence of "hydatid sand" within the cyst (Fig. 4). Ten cysts showed the multicystic or cyst within a cyst pattern and eight of these were found to contain daughter cysts at surgery. Three cysts displayed the ultrasonographic water lily sign and were found to contain nothing other than germinal membrane at surgery. A further three cysts showed evidence of hydatid sand resulting in a layer of fine echoes at the lower-most portion of the cyst. The aspirate from these cysts was found to contain unusually high quantities of sediment.

Group 3 cysts showed partial or total loss of the characteristic ultrasound features described in groups 1 and 2. They exhibited peripheral or diffuse distribution of coarse high amplitude echoes and generally had ill-defined borders. Some of these cysts also showed small cystic areas which were considered to be most likely due to daughter cysts (Fig. 5). At surgery these cysts were found to be secondarily

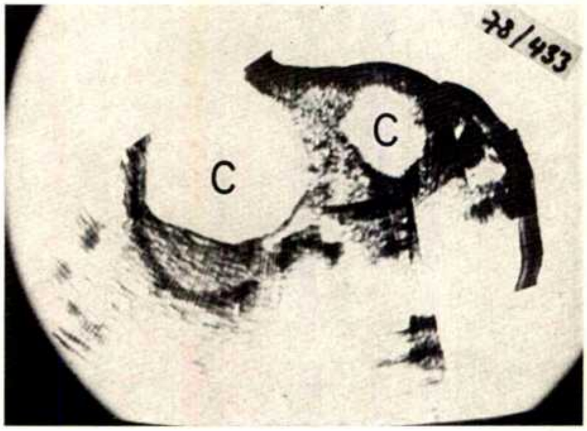


FIG. 1.

Transverse liver scan showing two completely anechoic hydatid cysts in the right and left lobes. C = Hydatid cyst.

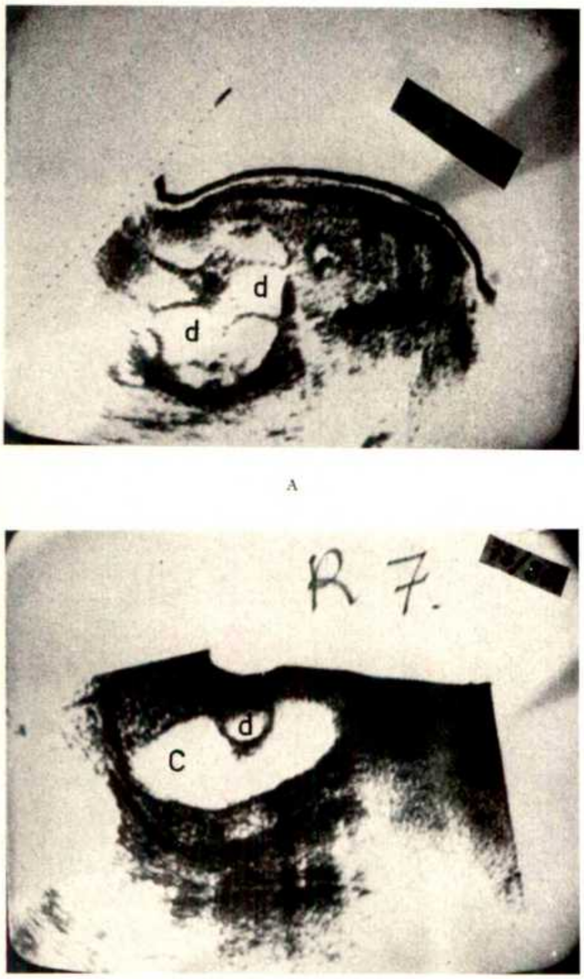


Fig. 2.

(A) Transverse liver scan showing multicystic mass in the right lobe (B). Liver hydatid cyst showing cyst within a cyst pattern. C = Hydatid cyst, d = daughter cyst.

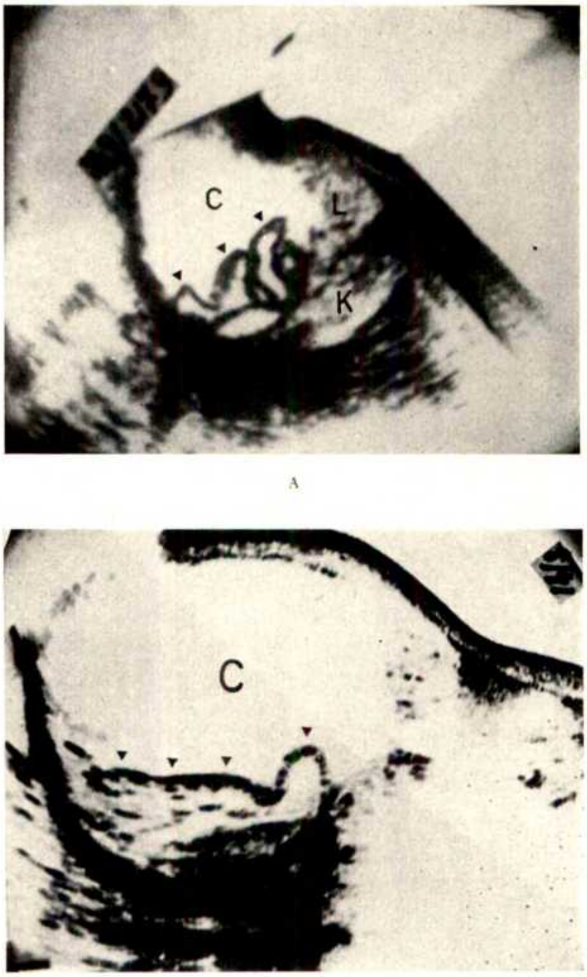


Fig. 3.

(A) Longitudinal scan of the liver hydatid cyst showing characteristic "water lily sign". At surgery these cysts are found to contain only germinal membrane. C = Cyst, L = Liver, K = Kidney. (B) In the supine longitudinal scan of the liver undulating echoes are seen at the lowermost portion of a cyst cavity (arrow heads) due to sunken detached germinal membrane, the ultrasonographic "water lily sign".

infected and contained viscid material. Nine cysts in eight patients exhibited these characteristics.

Discussion

The majority of our cases displayed the well-recognized ultrasound pattern of a simple cyst. Surprisingly we did not encounter a case of simple developmental cyst of the liver in this series of patients and were therefore unable to compare the ultrasound findings in these two different conditions. Previous descriptions and illustrations of simple cysts (King, 1973; Weaver *et al.*, 1978; Wooten *et al.*, 1978; Spiegel *et al.*, 1978), show ultrasonic characteristics similar to our group 1 hydatid cysts and we have been unable to identify any distinguishing features of hydatids showing this ultrasound pattern. Other cystic lesions of the liver, including haematoma and abscess, may also mimic this appearance (Spiegel *et al.*, 1978).

The multicystic appearance or cyst within a cyst pattern is accepted as characteristic of hydatid disease (King, 1973). It has been generally accepted that this pattern is due to the presence of daughter cysts within the primary cyst (King, 1973; Babcock

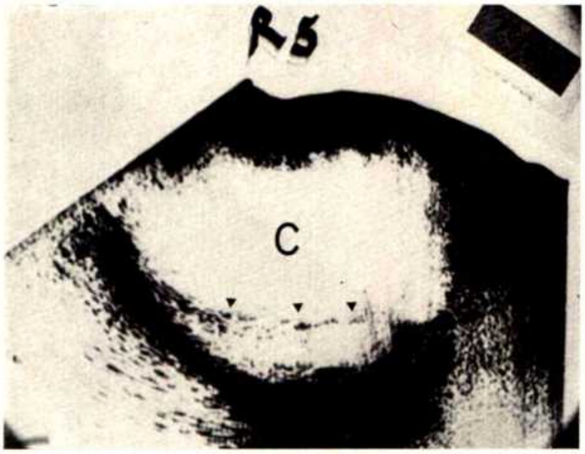


FIG. 4.
Longitudinal scan of a liver hydatid cyst showing layering fine echoes at the lowermost portion of the cyst cavity most likely representing hydatid sand (arrow heads).

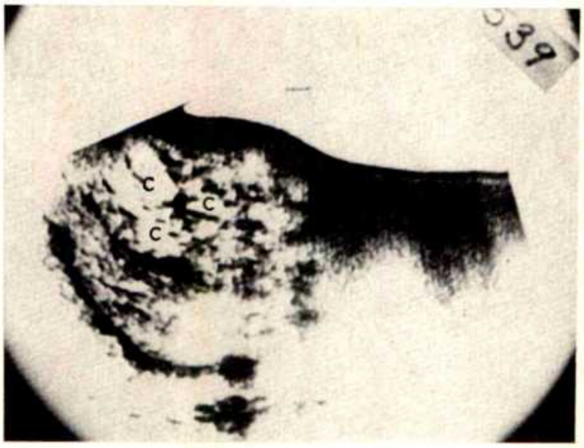


FIG. 6.
Longitudinal scan of multicystic masses in the right lobe of the liver. Surgically these lesions were found to be multiple small cysts closely gathered in an area and separated from each other by thin fibrotic liver tissue. C = Cyst.

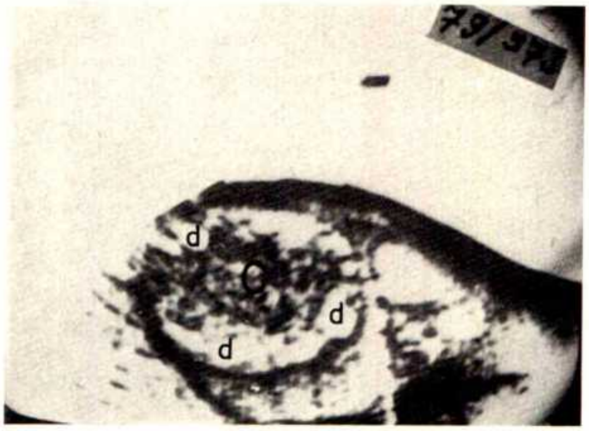


FIG. 5.
Longitudinal scan of the liver showing an infected hydatid cyst in the right lobe which has centrally located dense echoes and small cystic areas in its periphery due to daughter cysts (d).

et al., 1978) but no daughter cysts were seen in our two cases with a multicystic appearance ultrasonically. At operation the surgeon found multiple small cysts closely related to each other within the liver but separated from one another by attenuated and fibrotic liver tissue (Fig. 6). We therefore feel that this appearance should be interpreted cautiously before being accepted as a characteristic feature of daughter cysts. The formation of daughter cysts is not considered to be a normal part of the parasitic life cycle. They are normally only produced when the continued survival of the primary cyst is threatened. Such a threat may take the form of mechanical, chemical (bile in liver cysts or urine in kidney cysts) or bacterial insult (Poole and Marcial-Rojas, 1975). This probably explains why the majority of hydatid cysts do not show this appearance. The new sign proposed by us, "the ultrasonographic water lily sign" is due to detachment and collapse of the germinal layer and is analogous to the appearance seen in a chest X ray when a hydatid cyst has ruptured into the bronchial tree. Ultrasonically the collapsed germinal layer is seen as an undulating linear collection of echoes either floating in the cyst fluid or lying in the most dependent portion of the cyst (Fig. 3A, B). The pressure of the cyst fluid normally prevents detachment of the germinal membrane from the cyst wall. However, following surgical puncture of the cyst the pressure is reduced and collapse of this layer usually occurs. We may therefore presume that the ultrasound pattern we describe results from leak of fluid from the cyst by one of many routes, possibly biliary or portal, leading to subsequent collapse of the germinal layer. We have observed a similar appearance in a splenic hydatid cyst which was punctured inadvertently before ultrasonic examination.

Large numbers of brood capsules and freed scolices may be present within the cyst fluid and have been termed "hydatid sand" (Poole and Marcial-Rojas, 1975). We encountered three cysts in which ultrasound examination revealed a layer of fine echoes at the bottom of the cyst cavity which exhibited free movement with change in the patients position. This finding is, however, of limited diagnostic significance since debris within an abscess or

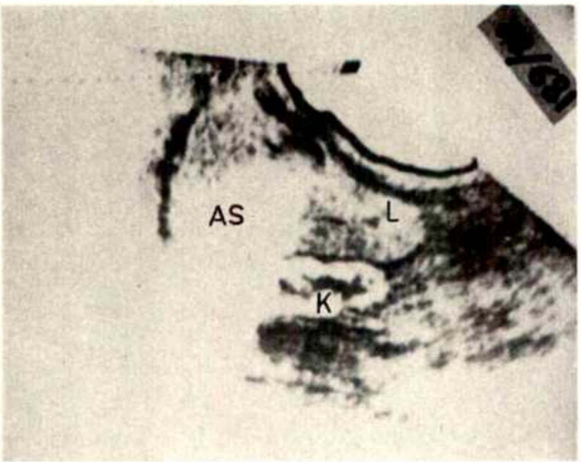


Fig. 7.

Echo complex of a calcified hydatid cyst. Curvilinear dense echoes representing the anterior wall of the calcified cyst in the anterior portion of the liver (L), and posterior acoustic shadow (AS), K = Kidney.

necrotic tumour could also produce a similar ultrasound appearance.

The cysts in group 3 exhibited both central and peripheral highly reflecting structures In addition some showed small cystic areas and at operation all these cysts were found to be secondly infected, to have formed fistulae or show localized areas of calcification. Aspiration of these cysts was generally impossible owing to the high viscosity of the cyst material. Secondary infection probably occurs via the blood or biliary system and a variety of organisms have been reported including salmonella and other pyogenic bacteria (Belding, 1965). The ultrasonographer who is unfamiliar with the less typical features of liver hydatid disease will find it particularly difficult to establish a correct differential diagnosis in these cases unless typical uncomplicated cysts are seen elsewhere within the liver. Three cysts in our series were totally calcified and produced the non-specific ultrasound pattern of massive acoustic shadowing (Fig. 7). The diagnosis was confirmed by the characteristic X-ray appearances.

Our experience leads us to conclude that the diagnostic accuracy of ultrasound in liver hydatid disease can approach 100%. If abdominal hydatid disease is clinically suspected ultrasound should be chosen as the first method of investigation.

REFERENCES

Alltree, M., 1979. Scanning in hydatid disease. *Clinical Radiology*, *30*, 691–697.

Babcock, D. S., Kaufman, L. and Cosnow, I., 1978. Ultrasound diagnosis of hydatid disease (echinococcosis) in two cases. *American Journal of Roentgenology*, *131*, 895–897.

Belding, D. L., 1965. Echinococcus granulosus. In *Textbook of Parasitology* (Appleton-Century-Crofts, New York), pp. 626–643.

Garrett, W. J., Kossoff, L., Uren, R. F. and Carpenter, D. A., 1976. Grey scale ultrasonic investigation of focal defects on ^{99m}Tc sulphur colloid liver scanning. *Radiology*, *119*, 425–428.

King, D. L., 1973. Ultrasonography of echinococcal cysts. *Journal of Clinical Ultrasound*, *1*, 64–67.

Poole, J. B., Marcial-Rojas, R. A., 1975. Echinococcosis. In *Pathology of Protozoal and Helmintic Disease with Clinical Correlation*, (Robert E. Krieger, Huntington/New York), pp. 635–656.

Spiegel, R. M., King, D. L. and Green, W. M., 1978. Ultrasonography of primary cyst of the liver. *American Journal of Roentgenology*, *131*, 235–238.

Taylor, K. J. W., Carpenter, P. A., Hill, C. R. and McCready, V. R., 1976. Grey scale ultrasound imaging: the anatomy and the pathology of the liver. *Radiology*, *119*, 415–423.

Weaver, R. M., Goldstein, H. M., Green, B. and Perkins, C., 1978. Gray scale ultrasonographic evaluation of hepatic cystic disease. *American Journal of Roentgenology*, *130*, 849–852.

Wooten, W. B. Green, B. and Goldstein, H. M., 1978. Ultrasonography of necrotic hepatic metastases. *Radiology*, *128*, 447–450.

1981, *British Journal of Radiology*, *54*, 339–340 APRIL 1981

Case reports

Encysted peritoneal hydatidosis, unusual ultrasonographic and clinical presentation of liver echinococcosis

By E. A. Niron, M.D., H. Özer, M.D., and H. Dolunay, M.D.

Department of Radiology, Aegean University, Faculty of Medicine, Izmir, Turkey

(*Received June 1980 and in revised form September 1980*)

Encysted peritoneal hydatidosis is an unusual manifestation of liver echinococcosis. We are not aware of any previous reports in the English literature of the grey scale ultrasound findings in this condition and present here two proven cases.

CASE REPORTS

Case 1

A 16-year-old girl with a long-standing history of a protuberant lower abdomen had experienced severe abdominal pain radiating to the left shoulder for the two days prior to her admission to hospital. Ultrasonography revealed a large cystic mass which was presumed to be a giant ovarian cyst. At surgery a large hydatid cyst was found originating from the pelvic wall and was successfully removed. Five months later the patient was re-admitted with diffuse abdominal swelling which gave the clinical impression of ascites. Repeat ultrasound examination again revealed a massive totally anechoic cyst occupying the entire abdominal cavity (Fig. 1). In addition an ill-defined cystic area was found in the left lobe of the liver. Isotope liver scan confirmed the presence of this defect. At surgery a large cystic mass was found with attachments to the anterior abdominal wall, omentum, spleen and left hemidiaphragm. The cyst contained 3.5 l of bile stained fluid and communicated directly with the cystic cavity within the liver.

Case 2

A 38-year-old male was admitted to hospital with a history of two years abdominal swelling and fatigue having been treated unsuccessfully for presumed tuberculous peritonitis and cirrhosis. Clinical examination revealed the physical signs of free peritoneal fluid but several attempts at paracentesis were unsuccessful. The Casoni test was positive while the Weinberg test was negative. Ultrasonography revealed a multicystic mass in the right lobe of the liver and multiple cystic structures of differing sizes throughout the entire abdomen (Fig. 2). At surgery a large hydatid cyst was found within the liver which communicated directly with a massive intra-abdominal extension. Both the liver cyst and its extension contained numerous daughter cysts. The primary cyst was successfully removed and contained 4 l of fluid.

DISCUSSION

The liver is infested in approximately 60% of cases of human hydatid disease (Romeo-Torres and Campbell, 1965). Liver hydatid cysts may rupture into various organs or spaces or may remain unruptured and calcify (Bonakdarpour, 1967). Rupture of cysts into the biliary tree may occur in 5–10% of cases (Schwartz, 1974; Macris and Galanis, 1966). Cysts may also rupture into the free peritoneal cavity and produce peritonitis and metastatic seeding. In a review of 223 cases of hydatid disease 30 instances of peritoneal spillage at the time of surgery have been documented (Schiller, 1966).

Extension of the intact liver cyst into the peritoneal cavity, encysted peritoneal hydatidosis, is rare. We

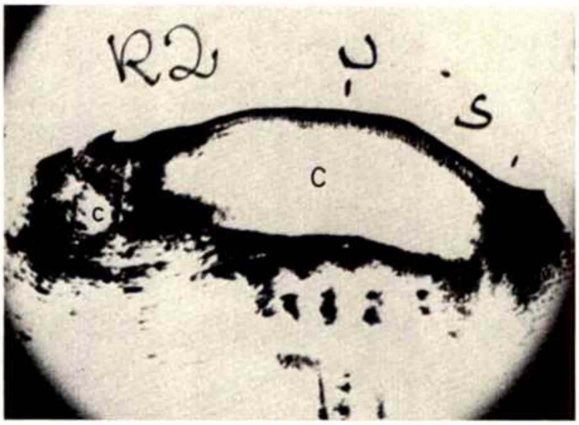


FIG. 1.

Longitudinal scan 2 cm to the right of the mid-line showing a cystic mass occupying the entire abdomen (C). An ill-defined cavity is also seen within the left lobe of the liver (c).

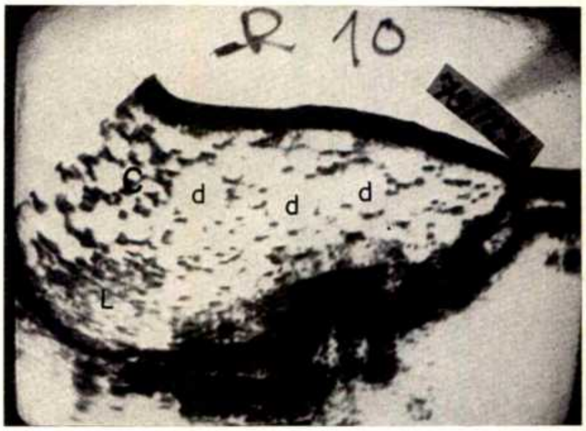


FIG. 2.

Longitudinal scan 10 cm to the right of the mid-line showing a large multicystic mass (C) with multiple daughter cysts (d) throughout the abdomen. A small portion of the liver is also seen (L).

1981, *British Journal of Radiology*, *54*, 340–342

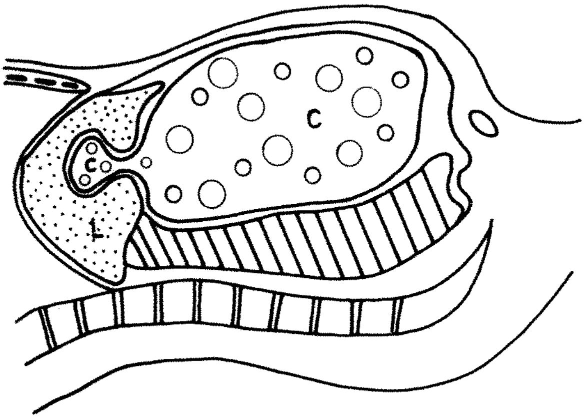


FIG. 3.

Diagrammatic representation of the encysted peritoneal echinococcosis. c = intra-hepatic portion of the hydatid cyst. C = intra-abdominal extension of the cyst. L = liver.

have encountered only two cases in almost 75 patients in whom ultrasound has demonstrated liver hydatid disease. In this condition the wall of the liver cyst extends into the peritoneal cavity with all its layers intact and covers the inner surface as though it were a second peritoneum (Fig. 3). There is no peritoneal spillage or implantation. This disorder has also been termed heterotopic peritoneal echinococcosis (Goinard *et al.*, 1960).

Ultrasonically this condition is seen as either an anechoic or multiloculated cystic mass occupying the entire abdomen. The intra-hepatic portion of the cyst and the communication with the abdominal component may also be demonstrated.

In our experience ultrasonography is the most valuable and accurate method for detecting the size, number and location of hydatid cysts and their complications.

REFERENCES

BONAKDARPOUR, A., 1967. Echinococcus disease. *American Journal of Roentgenology Radium Therapy and Nuclear Medicine*, *99*, 660–667.

GOINARD, P., PEGULLO, J. and PELISSIER, G., 1960. Hydatidose péritonéale. In *La kyste hydatique* (Masson, Paris), pp. 74–80.

MACRIS, G. J. and GALANIS, N. N., 1966. Rupture of echinococcus cyst of the liver into the biliary ducts. *American Surgeon*, *32*, 36–44.

ROMEO-TORRES, R. and CAMPBELL, J. R., 1965. An interpretive review of the surgical treatment of hydatid disease. *Surgery Gynecology and Obstetrics*, *121*, 851–864.

SCHILLER, C. F., 1966. Complications of echinococcus cyst rupture. *Journal of American Medical Association*, *195*, 220–222.

SCHWARTZ, S. I., 1974. Liver. In *Principles of Surgery*, Ed. S. I. Schwartz, (McGraw-Hill, New York), pp. 1177–1220.

Acetabulum excavatum in adult Down's syndrome

By G. Evison, F.R.C.R. and Margaret Oliver, D.C.R.

Department of Radiology, Shepton Mallet District Hospital

(Received July 1980 and in revised form October 1980)

Pelvic abnormalities in children with Down's syndrome (mongolism, trisomy 21) are well recognized. Recent attention has been drawn to the appearances of the pelvis in adults with this condition (Roberts *et al.*, 1980). We report here the case of an adult mongol who has developed unusual features in one hip, not previously recorded in this condition.

CASE REPORT

The patient is a 33-year-old woman with Down's syndrome, who has been in an institution since the age of seven. She suffers from severe mental subnormality, and unlike most patients with this condition, has throughout her stay been aggressive and disruptive, prone to sudden violence, and for many years doubly incontinent, with disgusting personal habits. She did not walk until about ten years ago, at the age of 23, preferring to lie on her back and wave her legs about. In particular, she developed the habit of waving the right leg around in a circular way—"like a seal's flipper" was the nursing description.

For the past ten years she has walked a little, but always with a waddling gait, and this has become more noticeable recently, leading to her first radiographic examination. An AP radiograph of the pelvis (Fig. 1) shows expansion of the right acetabulum, which has a well-corticated margin. Measurements of the iliac index described by Caffey and Ross are not accurate in the adult because of the disappearance of the Y cartilage (Roberts *et al.*, 1980). In our case, a combination of this factor with the high but horizontal roof of the acetabulum and the splaying of the ilium precluded any worthwhile measurements. AP views of the right hip in internal rotation (Fig. 2A), external rotation (Fig. 2B) and with traction applied to the right leg (Fig. 2C), show the range of movement of the femoral head within the ballooned acetabulum.

The left femoral head shows avascular necrosis, with changes of osteoarthrosis in the left hip joint.

DISCUSSION

Abnormalities in the pelvis in patients with Down's syndrome were first recorded by Caffey and Ross in 1956, and in more detail in 1958. They include wide splaying of the iliac wings, coxa valga and elongation of the ischia, with rotation of the axes of the ilium and acetabulum from their normal, towards the horizontal plane.

Kaufmann and Taillard (1961) extended their study of 57 patients into young adult life, but the oldest patient in their series was 22 years. More recently, Roberts *et al.* (1980) have studied radiographs of the pelvis in 66 adult subjects with Down's syndrome. They found that only 38% had the classical pelvic shape associated with Down's syndrome in infancy and childhood. A variety of appearances was found in these adult pelves, which tended to be smaller than normal. Subluxation of the hip, which had been thought by Kaufmann and Taillard (1961) to be more common in the adult Down's syndrome patient, was found by Roberts *et al.* to be very uncommon, as was the incidence of osteoarthrosis.

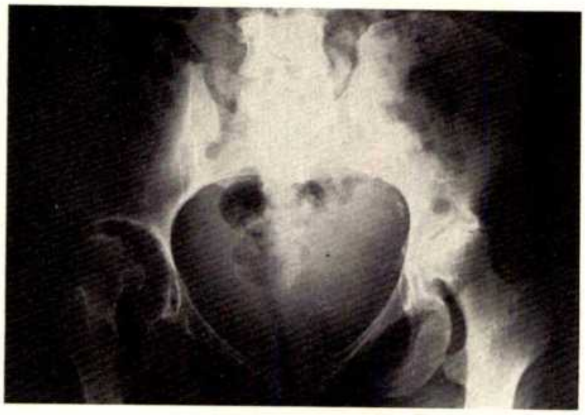
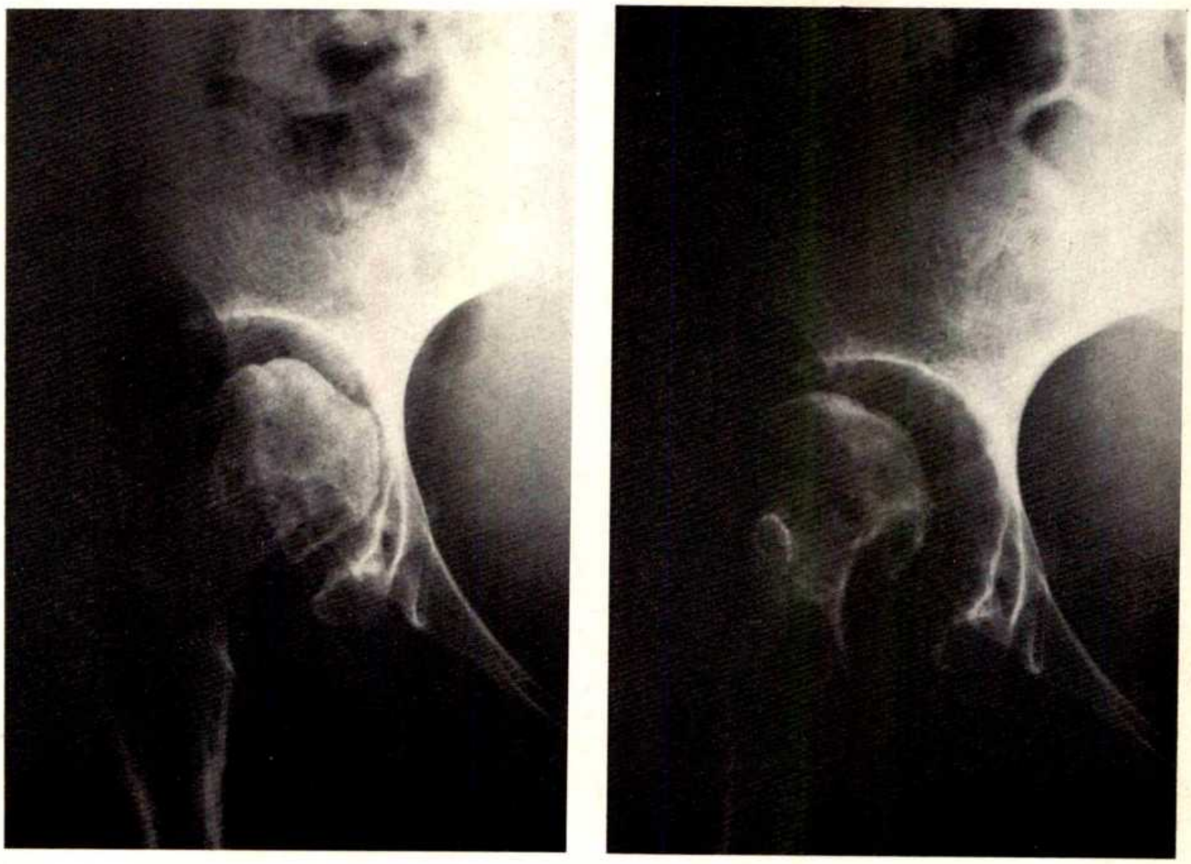


Fig. 1.

AP pelvis showing expanded acetabulum on the right, and avascular necrosis of the left femoral head, with secondary osteoarthrosis.

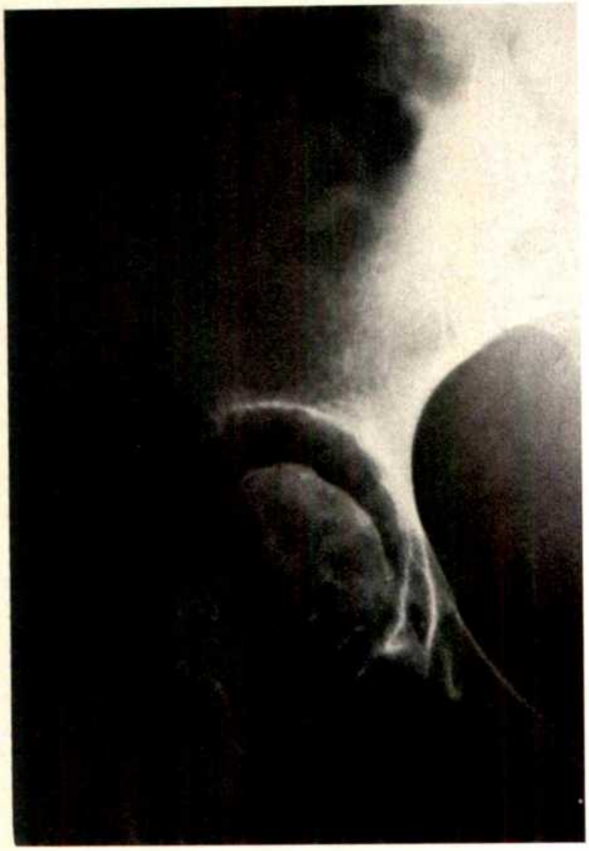
The present case shows several unusual features. The right acetabulum has been hollowed or scooped out, an appearance which we have called "acetabulum excavatum" and which, as far as we are aware, has not been recorded. Some reaming out of the acetabulum has been noted in patients in whom a metallic object, such as the protruding end of a Smith Petersen pin, has gouged a large cavity for itself within the acetabulum. In the present case, it appears that it was the femoral head itself which produced this effect.



A

Fig. 2.

B



C

FIG. 2.

AP of right hip. (A) Right leg internally rotated. (B) Right leg externally rotated. (C) Traction on right leg.

The absence of weight-bearing for 23 years, coupled with the rotational movements of the head of the femur during the "flipper hip" activity, is presumably responsible. The femoral shaft is narrower on this side, and hypoplastic, similar to the appearances following poliomyelitis, but there is no evidence of this having occurred in this patient.

There is a superficial resemblance to the acetabular enlargement sometimes seen in neuropathy and analgesic arthropathy. However, as far as can be clinically determined on this patient, there is no evidence of sensory deficit, and the patient had not been on any analgesics other than those prescribed from time to time for minor ailments. The Wassermann reaction is negative.

The right femoral head itself is small, but otherwise relatively normal, in contrast to the left which shows extensive avascular necrosis with osteoarthrosis in the hip. Roberts *et al.* (1980) found only seven cases with osteoarthrosis, out of a total of 66, and all of the mildest degree.

The ballooning of the acetabulum is not due to absorption following tuberculosis—the "expanded acetabulum" of Brailsford (1945, p. 147), as its margins are well-defined and corticated, with no evidence of previous bone destruction. Nor is it the "wandering acetabulum", described in osteoarthritis (Brailsford, 1945, p. 153). We would agree with the conclusion of Roberts *et al.* (1980) that, in addition to the primary morphological abnormalities in the pelvis in Down's syndrome, posture probably plays a part in producing the variable radiological appearances found in the pelvis.

ACKNOWLEDGMENTS

We are grateful to Dr. C. Howes and Dr. A. G. Blandford for clinical details; the Matron and staff of the Norah Fry Hospital for their help; Mrs. Barbara Stentaford for the typescript and Mrs. Sally Jenner for the illustrations.

REFERENCES

BRAILSFORD, J. F., 1945. *The Radiology of Bones and Joints* (J. and A. Churchill Ltd., London), pp. 147, 153.

CAFFEY, J. and ROSS, S., 1956. Mongolism during early infancy—some newly-recognised diagnostic changes in the pelvic bones. *Paediatrics*, *17*, 642–650.

1958. Pelvic bones in infantile mongolism. *American Journal of Roentgenology*, *80*, 458–467.

KAUFMANN, H. J. and TAILLARD, W. F., 1961. Pelvic abnormalities in mongols. *British Medical Journal*, *i*, 948–949.

ROBERTS, G. M., STAREY, N., HARPER, P. and NUKI, G., 1980. Radiology of the pelvis and hips in adults with Down's syndrome. *Clinical Radiology*, *31*, 475–478.

Colonic polyps in an infant following necrotizing enterocolitis

By C. Dicks-Mireaux, M.R.C.P., D. G. Shaw, F.R.C.P., F.R.C.R. and C. Fisher, M.R.C.Path.

Departments of Radiology and Pathology, University College Hospital, Gower Street, London WC1

(Received September 1980)

Polypoid lesions of the colon in childhood may be commonly due to lymphoid hyperplasia and are a feature of the juvenile polyposis syndrome and such rare diseases as familial polyposis, Gardner's, Peutz-Jeghers, Cronkhite-Canada and Turcot Syndromes. Regenerative polyps of ulcerative colitis

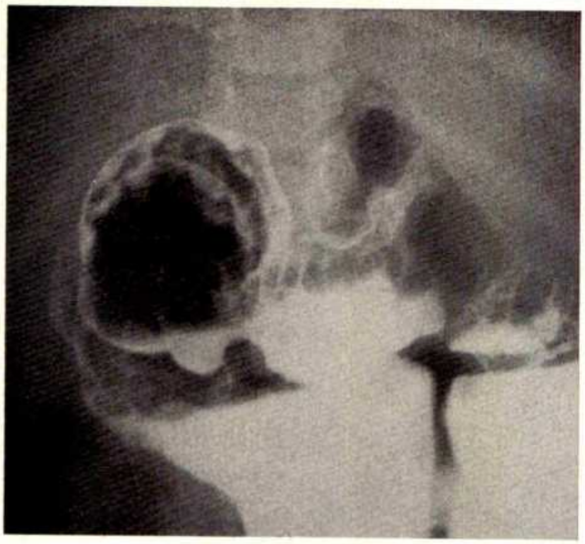


Fig. 1.
Radiograph of barium enema showing polyps in transverse colon.

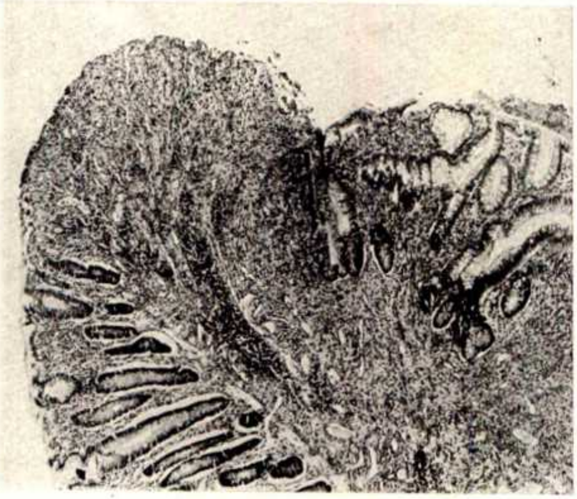


FIG. 2.
Photomicrograph of excised specimen from colon showing inflammatory polyp (haematoxylin and eosin, ×40).

are not common in early childhood. A child is reported in whom polyp formation is associated with colonic stricture secondary to neonatal necrotizing enterocolitis.

CASE REPORT

A caucasian female infant was born at 28 weeks' gestation with a birth weight of 980 g. Her mother, age 30, was admitted in labour with a 24-hour history of spontaneous rupture of membranes. The child was born by vaginal delivery with Apgar scores 4 (1 min) and 9 (5 min).

During her first week of life she had mild respiratory distress with apnoeic episodes. She was nursed in a head box with 35% oxygen and an umbilical arterial catheter was inserted. She was found to be septicaemic with a group "B" haemolytic streptococcus and was treated with antibiotics. She also had a low haemoglobin with mildly abnormal clotting studies and required several blood transfusions. Initially she was maintained on parenteral fluids and at four days of age nasogastric tube feeding with raw expressed milk was commenced.

When 18 days old she passed bright red blood per rectum. Abdominal X ray showed narrowing of the transverse and descending colon with intramural gas and a diagnosis of necrotizing enterocolitis was made. Oral feeds were discontinued and she was maintained on parenteral alimentation.

At 19 weeks of age she was found to be producing copious amounts of nasogastric aspirate and a Gastrografin swallow demonstrated dilated loops of small bowel. A laporotomy was performed at which a terminal ileal stricture was found. This was resected.

From 11 months of age she had repeated episodes of subacute intestinal obstruction which responded to medical treatment. At 16 months a barium enema demonstrated a stricture in the transverse colon with numerous polyps in the ascending and transverse colon (Fig. 1). Her attacks of intestinal obstruction became more frequent and difficult to control with almost continuous diarrhoea, anorexia, abdominal pain and failure to thrive. She then had a laparotomy at which by-pass of the colonic stricture was performed. The intestinal mucosa adjacent to the stricture was noted to be polypoidal and specimens were sent for histology. The histology specimen showed four sessile polyps 0.5–1.2 cm diameter. These were described as inflammatory polyps with a core of inflamed granulation tissue covered by hyperplastic regenerating colonic mucosa and showing increased chronic inflammation in the adjacent lamina propria (Fig. 2).

DISCUSSION

This report describes the formation of inflammatory polyps in the proximal colon associated with a colonic stricture secondary to neonatal necrotizing enterocolitis. Strictures associated with necrotizing enterocolitis are known to occur, but this is the first case of polyp formation following necrotizing enterocolitis that we have seen. However, with the increasing incidence of survival of premature babies and increasing incidence of necrotizing enterocolitis this type of regenerative colonic polyposis in infancy may occur more often.

ACKNOWLEDGMENTS

We thank Mr. G. L. Bunton and Professor E. O. R. Reynolds for enabling us to describe this case.

1981, *British Journal of Radiology*, *54*, 344–348

Case reports

Osteopathia striata with sclerosis and thickening of the skull

By *M. R. Paling, M.R.C.P., F.R.C.R., I. Hyde, F.R.C.P.(E)., F.R.C.R. and N. R. Dennis, B.A., M.R.C.P.

Departments of Paediatric Radiology and Child Health, Southampton General Hospital

(*Received July 1980 and in revised form October 1980*)

Osteopathia striata is a rare bone dysplasia characterized by fine linear striations particularly affecting the metaphyses of the long bones. A case is described in which, in addition, the skull showed sclerosis and thickening of its vault and base. The ribs, spine and pelvis also showed sclerosis but without striations. This case also had an osteochondroma, an association described in two of the ten previously reported cases.

CASE REPORT

A 12-year-old girl had been seen by various specialists because of mild development retardation, dorsiflexion deformity of the toes, nasal obstruction, rhinorrhoea, conductive deafness and dental abnormalities requiring extraction of several teeth. Her father, a 60-year-old ship repairer, her mother, a 45-year-old housewife and her brother were all healthy, as were six paternal and two maternal half-siblings.

Her birth weight was 3.0 kg at term and infancy was uneventful. She was a quiet baby. She walked at 2½ years, began to talk at 5 years and attended a special school for the educationally sub-normal. Mild deafness was noted at 12 years and an audiogram showed a bilateral 20–40 decibel hearing loss across most of the audible frequency range, becoming more severe at higher frequencies.

Her height was 158 cm (75 percentile), weight 41 kg (25–50 percentile) and head circumference 58.5 cm (between three and four standard deviations above the mean for the age). There was parietal bossing of the skull, a very broad nasal bridge with para-nasal bossing (inner canthal distance 4 cm, outer 9 cm) and a slight downward slant to the eyes. The palatal arch was narrow owing to greatly widened alveolar ridges in which the upper teeth were irregularly placed. No cranial nerve abnormalities were detected. The neck was broad and the lumbar lordosis pronounced with prominence of the sacrum. The sternum had a keel-shaped upper half and a depressed lower half. The rib cage was asymmetrical, being more prominent on the right, but there was no scoliosis. There was valgus deformity of the elbows and knees. The hands were normally formed with normal flexion creases but with distally displaced axial tri-radii in both palms and six ulnar loops and four whorls on the finger tips. The feet were high-arched and the toes dorsiflexed, especially the big toes, which had short first metatarsals. Muscle tone and reflexes were normal. The clinical impression was of mild to moderate mental retardation but no formal psychological test results were available.

A routine blood count, calcium and phosphorus levels were normal but the serum alkaline phosphatase was elevated (800 IU/L, adult upper limit of normal 275). The chromosome examination showed a normal female karyotype.

Radiographic features

Fine longitudinal striations were present at the metaphyses of all the long bones, most striking at either end of the femur,

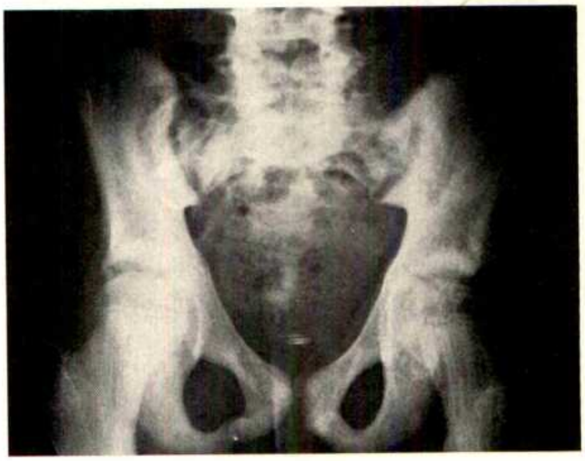


FIG. 1.

Increased density of the pelvis. Striations in the left ilium and upper femora. Anterior rotation of the iliac wings.

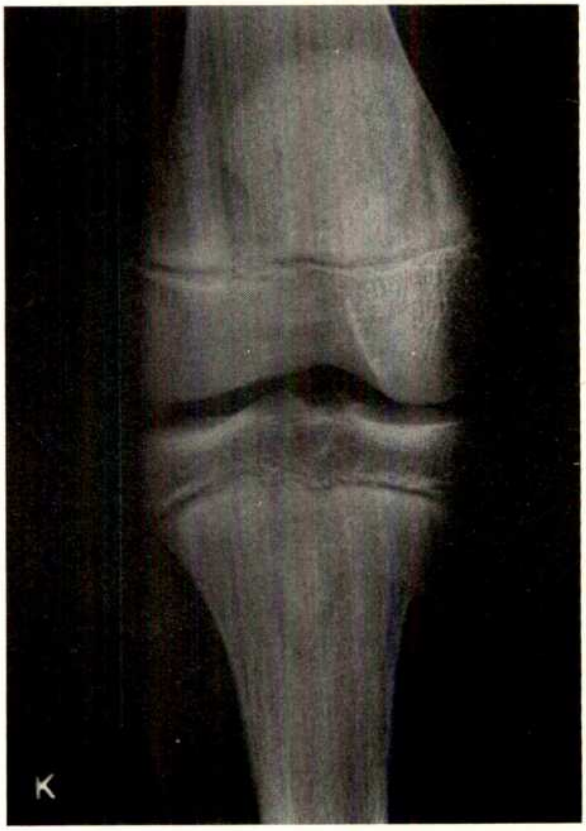


FIG. 2.

Metaphyseal striations. Osteochondroma at the upper tibia.

---

*Present address: National Institutes of Health, Bethesda, Maryland, USA.

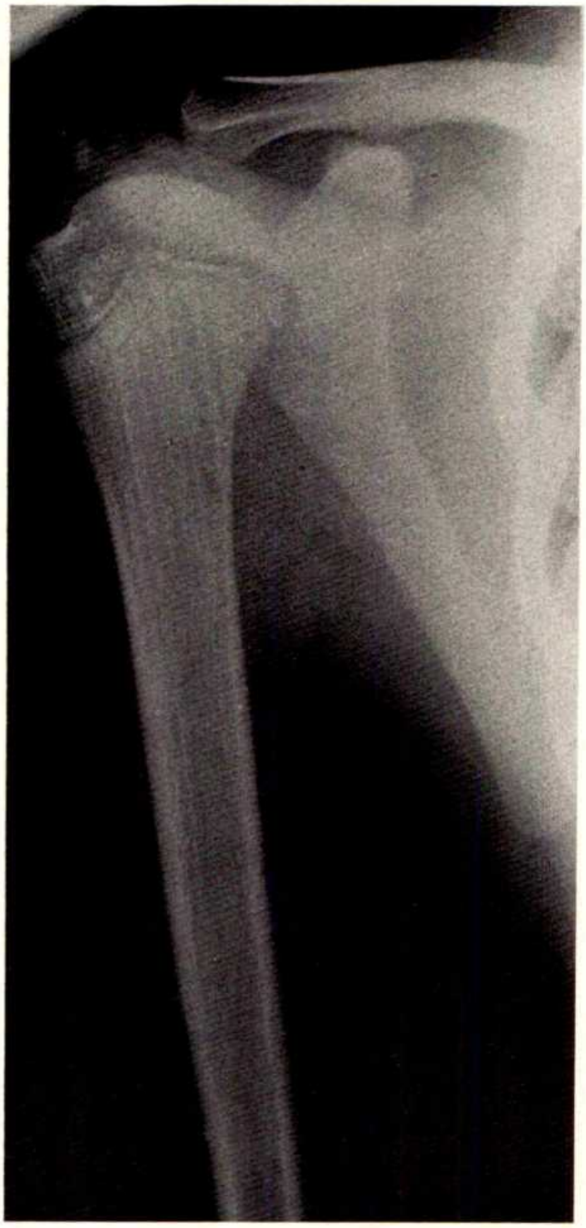
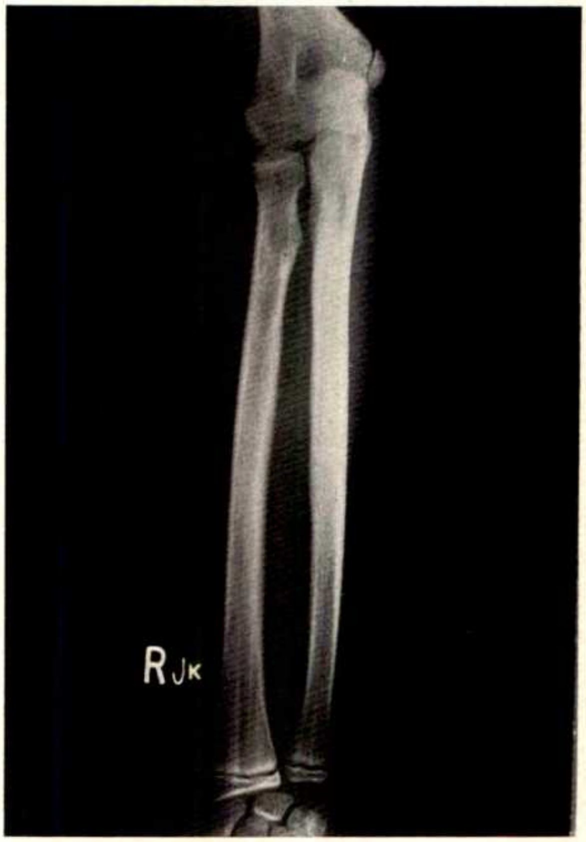


FIG. 3.
Metaphyseal striations.



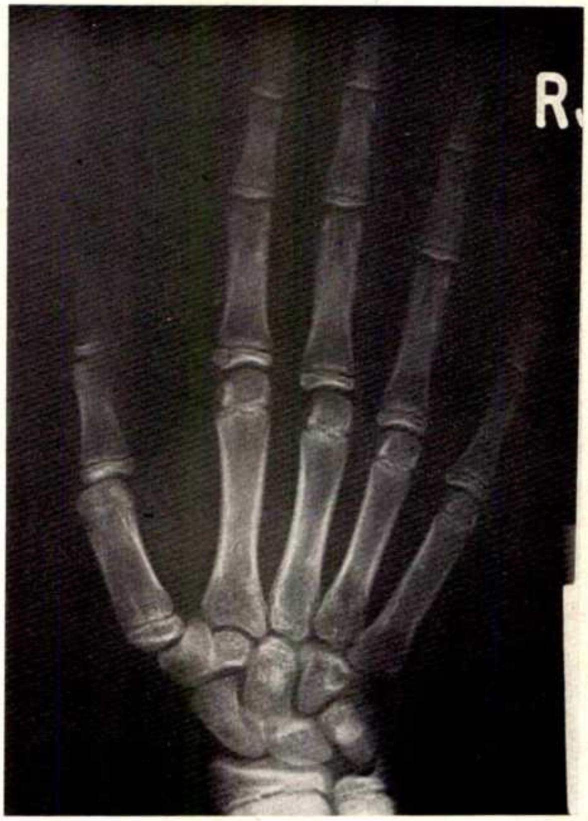


FIG. 4 (*above, right*).
Metaphyseal striations in the lower radius and ulna.

FIG. 5 (*below, right*).
Thickening of the metacarpal shafts.

the proximal tibia, the proximal humerus and at the distal radius and ulna (Figs. 1 to 4). The changes were bilateral and symmetrical. There was no deformity of the long bones but an osteochondroma arose from the upper right tibia (Fig. 2).

The carpus and tarsus were normal and there were no striations in the hands or feet but all the metacarpals showed abnormal modelling of their shafts (Fig. 5). The first metatarsal was short.

The skull was large with marked sclerosis and thickening of the vault and base (Figs. 6 and 7). The ribs were thickened but without striae (Fig. 8). All the vertebrae showed increased density but without striae. A spina bifida occulta was present at D12, L5 and S1. (Figs. 9 and 10).

The pelvis had increased density with faint striations in the iliac wings. It was narrow in the coronal plane due to anterior rotation of the iliac wings. (Fig. 1).

Radiographs of the patient's mother and father (skull and knee) were normal.

DISCUSSION

Osteopathia striata was first described by Voorhoeve (1924) in two children (a boy and a girl) and their father. The condition appeared to be asymptomatic apart from mild joint pains and crepitus. The boy was educationally backward, although thought by the author to be of normal intelligence.

Fairbank (1925) described a further case, a 12-year-old boy with awkwardness and slight overgrowth of the right leg, to which the radiological changes appeared to be confined. Later (Fairbank, 1950) less severe changes appeared on the left side.

Hurt (1953) reported a 51-year-old man described as "unintelligent" in whom the skeletal changes were an incidental finding. In addition to the fine longitudinal metaphyseal striations seen in the other cases of osteopathia striata, he also showed thickening and increased density of the skull and ribs.

Bloor (1954) reported a three-year-old girl with mental retardation and nasal obstruction, a large head, hypertelorism, a high arched palate but no deafness. The skull showed increased density of the base and frontal bones.

The next case, that of Jones and Mulcahy (1968), a 26-year-old woman, also showed thickening and sclerosis of the skull associated with deafness due to stenosis of the external auditory meatus and tympanic cavity. Neither the intelligence nor the facial appearance were mentioned.

Walker (1969) described a 20-year-old girl with a large head of unusual shape, thickened nasal bridge, borderline mental retardation, deafness due to stenosis of the auditory meatus, chronic otitis and incipient cataracts. The skull, especially the base, was thickened and dense.

Two further cases were reported by Gehweiler *et al.* (1973). The first was a 19-year-old mentally retarded girl whose osteopathia striata was brought to light because of minor skeletal symptoms. The second was a 24-year-old woman in whom the

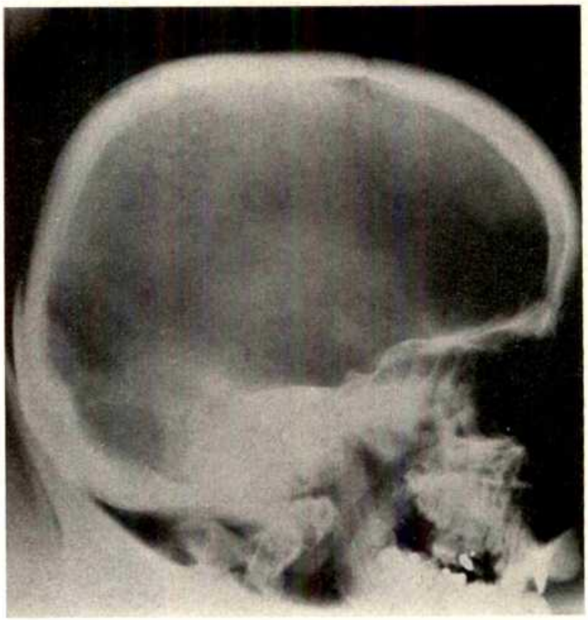


FIG. 6.

Thickening and increased density of the vault, base and facial bones.

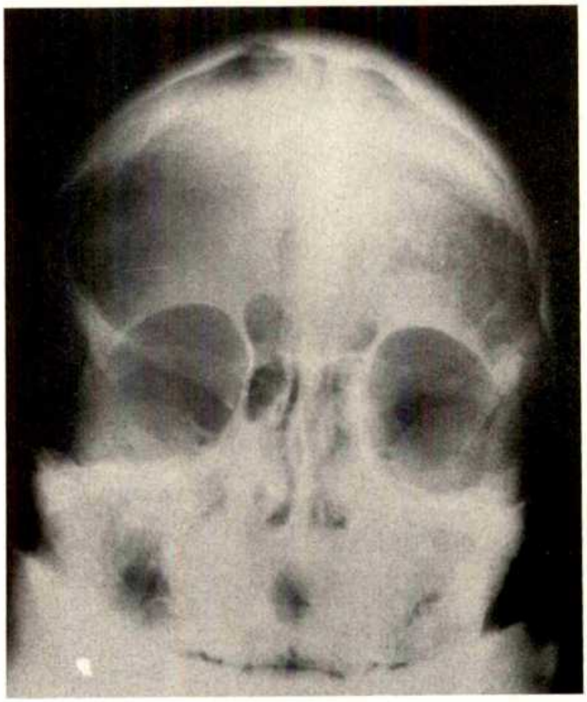
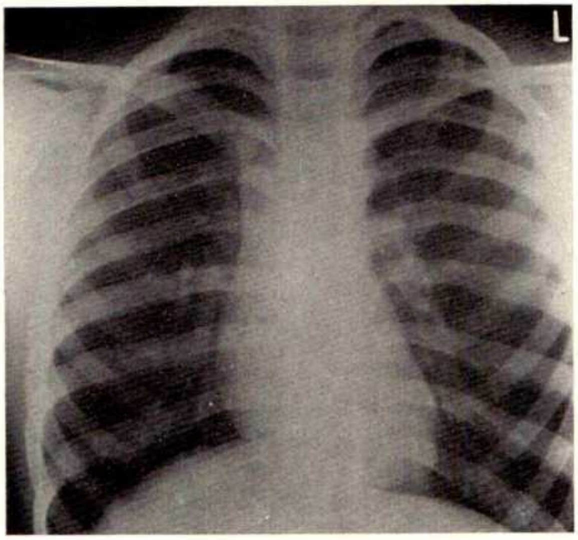
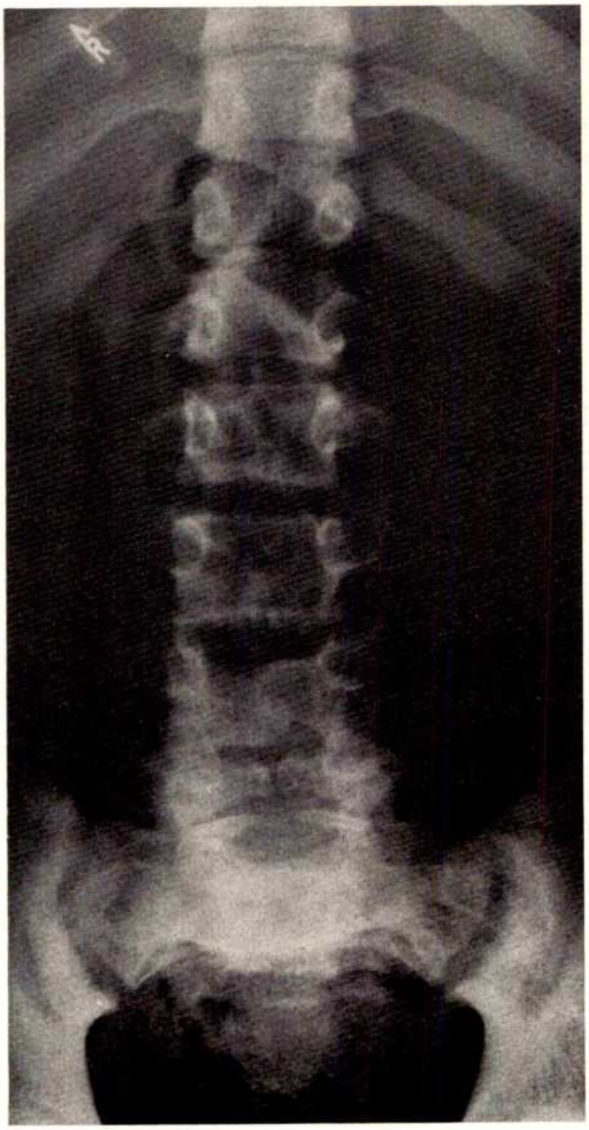


FIG. 7.

Thickening and increased density of the vault, base and facial bones.





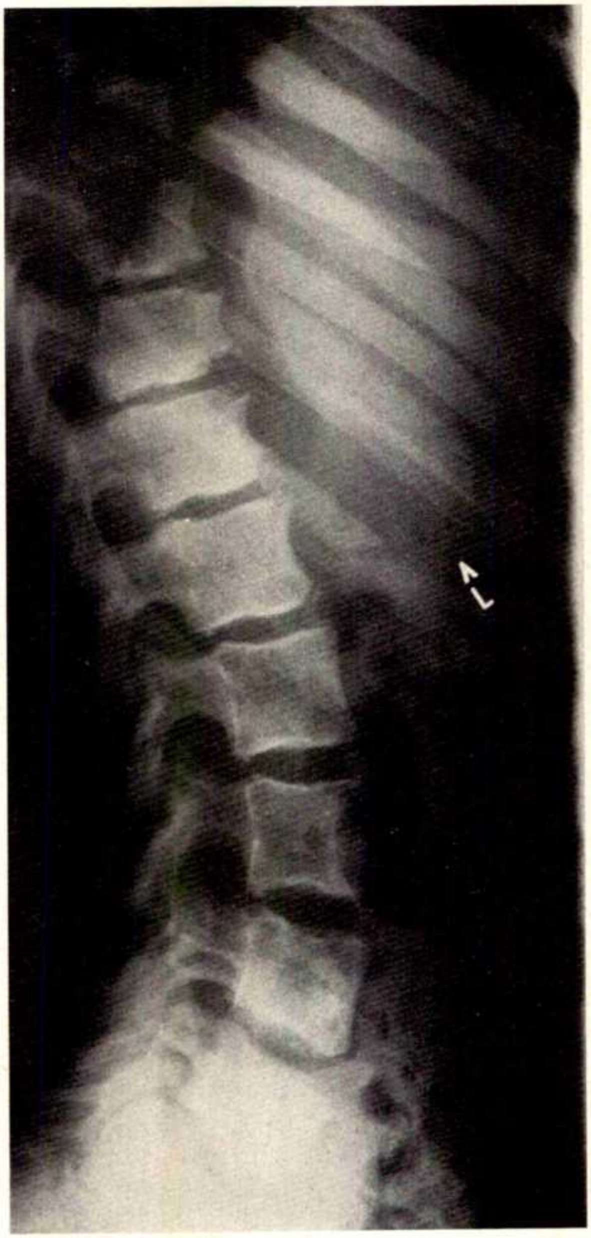


FIG. 10.
Spina bifida occulta of D12, L5 and S1. All the vertebrae have increased density.

FIG. 8 (*above, left*).
Ribs thickened and of increased density.

FIG. 9 (*below, left*).
Spina bifida occulta of D12, L5, and S1. All the vertebrae have increased density.

1981, *British Journal of Radiology*, *54*, 348–350

skeletal abnormalities were found incidentally while she was being treated for a psychiatric disorder. In neither case was thickening or sclerosis of the skull mentioned.

Apart from these 10, we are not aware of any other cases of osteopathia striata published with full description. There is general agreement that the finely striated appearance of the metaphyses of the long bones and sometimes of the pelvis and vertebrae is specific for this condition and distinguishable from the coarser striations seen in some other conditions. The three-generation family of Rucker and Alfidi (1964), sometimes quoted as osteopathia striata and called by them Fairbank's disease, appear to have a different condition akin to Fairbank's (1950) case seven and called therein hyperostosis generalisata with striation of bones.

Although osteopathia striata is sometimes a harmless incidental finding it is clear that it can be associated with mental retardation, nasal obstruction, conductive deafness due to bony encroachment on the ear canal and middle ear and possibly with cataracts. The narrowing of the optic foramina seen in the case of Walker (1969) also raises the possibility of optic nerve entrapment. The serious complications seem to be confined to the sub-group of patients with sclerosis and thickening of the skull. It is not clear whether these patients have a different disease from those with normal skulls as described by Voorhoeve (1924) and Fairbank (1925). Voorhoeve's family clearly showed autosomal dominant inheritance of a mild form of the disease. Beighton (1978) briefly mentions four families with skull involvement, also with autosomal dominant inheritance. The other cases, including ours, were sporadic, or the families were not investigated, so that it is impossible to assess the amount of intra-familial variation. It is interesting to note that all the cases with severe complications have been females, which may imply a sex difference in the expression of an autosomal dominant gene. The father of our patient was 48 years old at the time of her birth which suggests a new dominant mutation but in the absence of radiographs of other family members it is impossible to exclude mild disease amongst them.

Radiographic features of our case which have not previously been noted are shortening of the first metatarsals, thickening of the shafts of the metacarpals, spina bifida occulta and increased lumbar lordosis. Osteochondromata arising from the upper tibial metaphysis have been mentioned by other authors and are probably part of the radiological picture.

Osteopathia striata is a potentially serious condition if associated with sclerosis and thickening of the skull. Further family studies are needed to determine whether the mild and severe forms are genetically distinct.

ACKNOWLEDGMENT

We are grateful to Professor I. C. S. Normand for permission to report this case.

REFERENCES

BEIGHTON, P., 1978. Inherited disorders of the skeleton. (Churchill Livingstone, Edinburgh/London/New York), pp. 129–130.

BLOOR, D. U., 1954. A case of osteopathia striata. *Journal of Bone and Joint Surgery*, *36B*, 261–265.

FAIRBANK, H. A. T., 1925. A case of unilateral affection of the skeleton of unknown origin. *British Journal of Surgery*, *12*, 594–599.

1950. Osteopathia striata. *Journal of Bone and Joint Surgery*, *32B*, 116–125.

GEHWEILER, J. A., BLAND, W. R., CARDEN, T. S. and DAFFNER, R. H., 1973. Osteopathia striata—Voorhoeve's disease—review of the roentgen manifestations. *American Journal of Roentgenology*, *118*, 450–455.

HURT, R. L., 1953. Osteopathia striata—Voorhoeve's disease. *Journal of Bone and Joint Surgery*, *35B*, 89–96.

JONES, M. D. and MULCAHY, N. D., 1968. Osteopathia striata, osteopetrosis and impaired hearing. *Archives of Otolaryngology*, *87*, 116–118.

RUCKER, T. N. and ALFIDI, R. J., 1964. A rare familial systemic affection of the skeleton; Fairbank's disease. *Radiology*, *82*, 63–66.

VOORHOEVE, N., 1924. L'image radiologique non encore décrite d'une anomalie du squelette. *Acta Radiologica*, *3*, 407–427.

WALKER, B. A., 1969. Osteopathia striata with cataracts and deafness. *Birth Defects Original Article Series*, 295–297.

The fate of the valves of autogenous vein grafts

By *P. C. Clifford, F.R.C.S., †J. P. Woodcock, Ph.D. and *R. N. Baird, M.S., F.R.C.S.

Departments of *Surgery and †Medical Physics, Bristol Royal Infirmary

(Received September 1980)

Autogenous vein graft is still the best and most widely used material as arterial substitute. However, the factors influencing the long term patency rate of vein grafts remain obscure. One of these may be related to the fate of the venous valve leaflets which may remain unaffected or become fibrotic and cause stenosis. Normal valves, although reversed, cause no loss of lumen diameter and may be harmless whilst fibrotic valves are implicated in early graft failure (Szilaggi *et al.*, 1973; Mavor *et al.*, 1975). This failure may be caused by turbulence around the valve cusps (McNamara *et al.*, 1967). We report two cases of autogenous vein grafts, imaged by ultrasound, demonstrating firstly a non-mobile fibrotic valve and secondly a normal mobile valve, which was the site of turbulent flow.

CASE REPORTS

A 64-year-old man with femoropopliteal segment arterial disease underwent vein bypass grafting using autogenous long saphenous vein 28 months prior to being studied. His symptoms of intermittent claudication improved and he remained well at follow-up. During post-operative ultrasound study of his graft, using the ATL Duplex real-time scanner, a stenotic area was noted 10 cm below the proximal anastomosis. No flow disturbance was detected using the Doppler flowmeter attachment and Fig. 1 shows this area with a fibrotic valve cusp.

A 59-year-old man was seen ten years after implantation of a femoropopliteal autogenous vein graft. He complained of exercise-related pain around the knee and was referred for ultrasound assessment. The graft was fully patent, with good flow, and 25 cm above the knee a moving intraluminal shadow of a valve cusp was identified. In Fig. 2 the graft and the intraluminal valve are seen. Doppler haemodynamic studies in the proximity of the valve detected disturbed blood flow and, using the M mode facility, the moving valve cusp was clearly visible. The valve "click" was audible during the reverse flow phase.

DISCUSSION

Further studies are needed to clarify the fate of venous valve leaflets when placed reversed in an arterialized environment and these cases demonstrate that ultrasonic imaging is sensitive enough to detect valve cusps and their haemodynamic effects. The second case suggests that normal reversed valves may

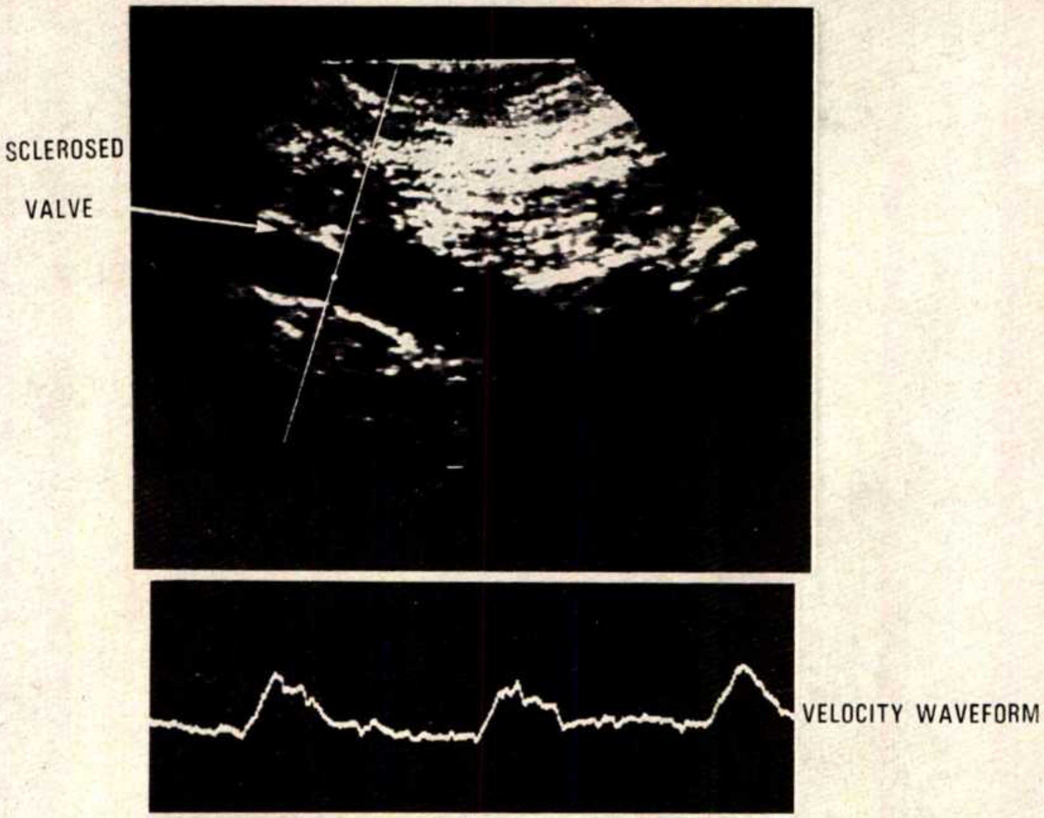


FIG. 1.

Real time ultrasound scan of a femoropopliteal vein graft demonstrating a fibrotic valve cusp but no flow disturbance.

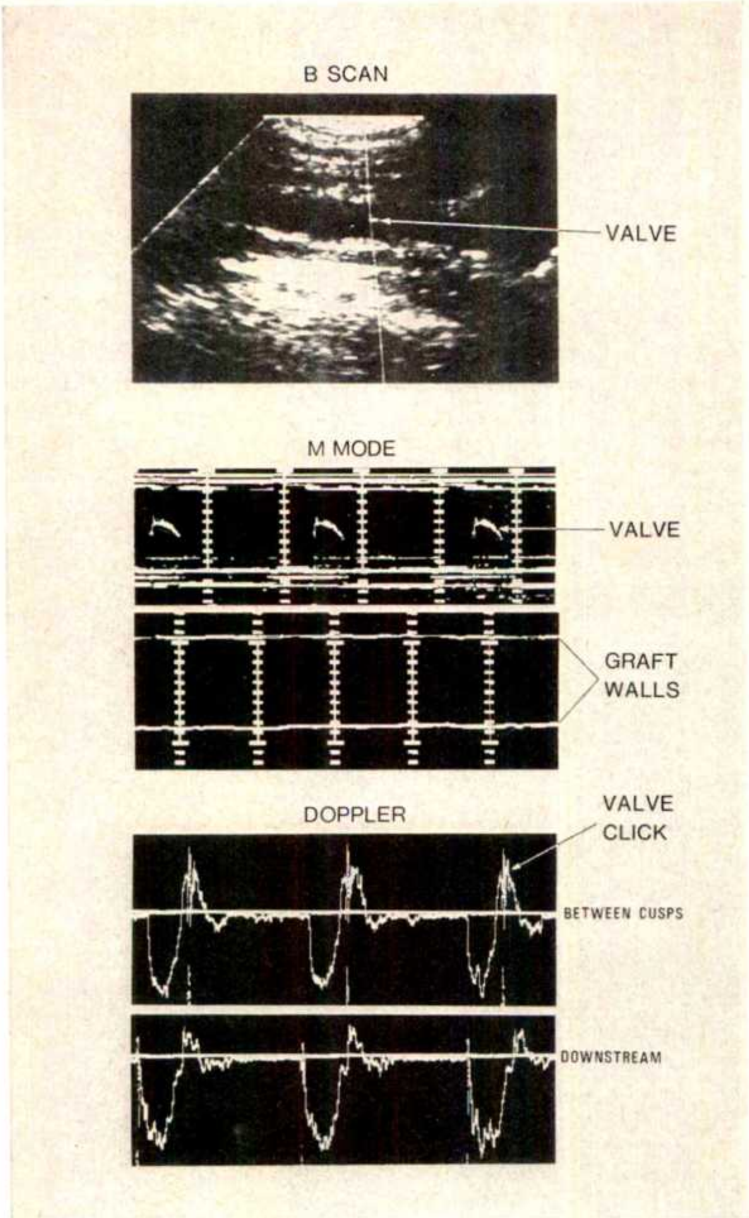


FIG. 2.

Real time B and M mode scans of a femoropopliteal vein graft with a reversed valve moving freely during systole and diastole. It was the site of flow disturbance detected by the Doppler flowmeter and produced a typical audible valve "click".

remain innocently in a graft for a long time despite being the site of flow disturbance.

ACKNOWLEDGMENT

P. C. Clifford is supported by British Heart Foundation Grant No. 717.

REFERENCES

Szilaggi, D. E., Elliott, J. P., Hageman, J. H., Smith, R. F., and Dall-Olmo, C. A., 1973. Biologic fate of autogeneous vein implants as arterial substitutes. *Annals of surgery*, *178*, 232–246.

McNamara, J. D., Darling, R. C., and Linton, R. R., 1967. Segmental stenosis of saphenous vein autografts. Preventable cause of late occlusion in arterial reconstruction. *New England Journal of Medicine*, *277*, 290–292.

Mavor, G. E., Krukowski, Z. H., Millar, D. G., Kasenally, A. T., and Woodruff, P. W. H., 1975. The long term behaviour of autogenous vein by-pass grafts. *Journal of Cardiovascular Surgery*, *16*, 130–134.

1981, *British Journal of Radiology*, 54, 351–352 APRIL 1981

Case reports

Ultrasonic demonstration of renal artery thrombosis

By P. Barber-Riley, M.B., Ch.B., M.R.A.C.R. and A. S. Patel, M.B., B.S., M.R.A.C.R.

Department of Diagnostic Radiology, Royal Perth Hospital, Perth, Western Australia

(*Received May 1980 and in revised form October 1980*)

The value of grey scale ultrasound in the diagnosis of thrombosis of the portal vein, renal veins and of the carotid artery has been established (Dunnick *et* al., 1979; Merritt, 1979; Schultze *et al.*, 1979).

We wish to report a patient with malignant hypertension in whom a diagnosis of renal artery thrombosis was made ultrasonically.

CASE REPORT

A 45-year-old woman was admitted for investigation of severe headache of four weeks' duration. Examination revealed a blood pressure of 290/120 mmHg, fundal haemorrhages and papilloedema. The rest of the physical examination was normal. The laboratory investigations indicated impaired renal function with elevated serum creatinine (231 mmol/l) and urea (20.1 mmol/l). The patient also had microscopic haematuria. Renal failure worsened despite adequate control of her blood pressure and the patient required haemodialysis.

An abdominal ultrasound examination was performed to assess the size of the patient's kidneys and to exclude the presence of a suprarenal tumour as the cause of her hypertension. This revealed a narrowed right renal artery with a thickened wall. The narrowed artery showed a low amplitude echo pattern within the lumen (Fig. 1). The appearances of the right renal artery were considered to be due to thrombosis. The left renal artery was patent and of normal calibre (Fig. 2). The kidneys were of normal size.

The arteriogram confirmed complete occlusion of the right renal artery, with collateral supply to the kidney. (Fig. 3A, B).

Right nephrectomy was performed and the presence of renal artery thrombosis with underlying atheroma was confirmed at surgery.

DISCUSSION

In the Royal Perth Hospital, abdominal ultrasound examination is carried out in selected patients with malignant hypertension. In these patients, ultrasound is useful in the detection of adrenal tumours. It is also used to exclude obstruction in hypertensive patients with non-functioning kidneys (Whalen, 1979). We feel ultrasound findings are relevant in the management of hypertensive patients and in rationalization of further investigations.

For adequate visualization of the renal arteries, the ultrasound examination needs to be performed in the supine position. Serial, closely spaced transverse scans in the long axis of the artery must be made to obtain a true assessment of the lumen. Real time

---

Address for reprints: Dr. P. Barber-Riley, Department of Diagnostic Radiology, Royal Perth Hospital, Perth, Western Australia.

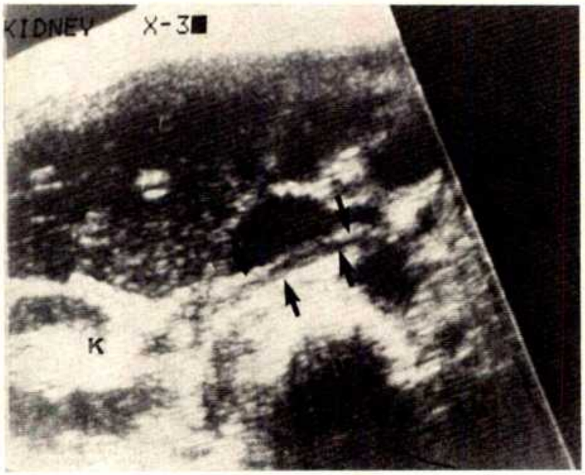


FIG. 1.

Supine transverse scan showing the narrowed right renal artery (arrows) with low amplitude echoes within it.

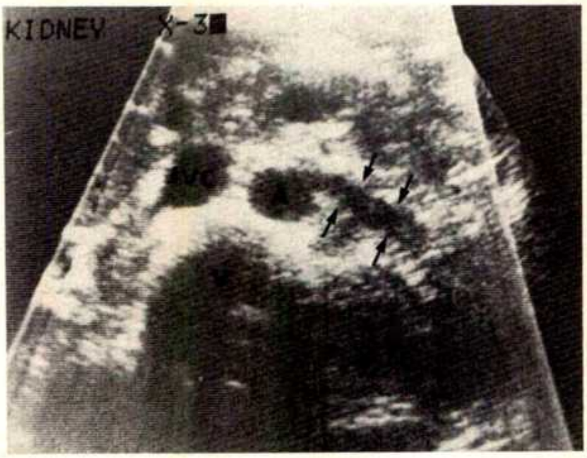


FIG. 2.

Supine transverse scan showing normal left renal artery. IVC, inferior vena cava; K, right kidney; A, aorta; V, vertebral body.

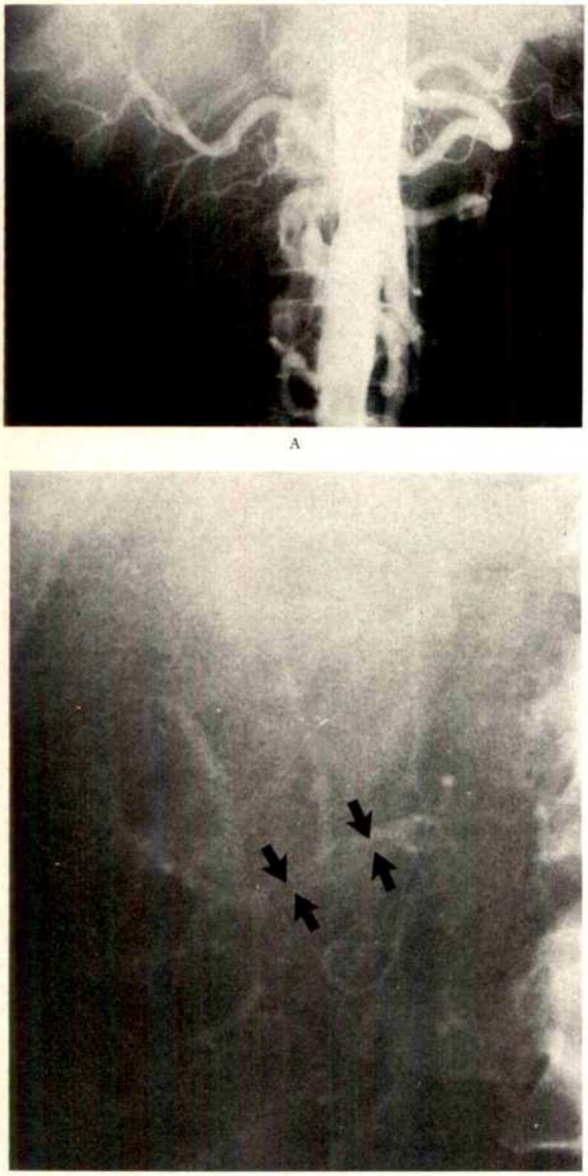


FIG. 3.

(A) Arterial phase of mid-stream aortogram showing no right renal artery filling.

(B) Late phase of mid-stream aortogram showing thrombus in the main right renal artery (arrows), and filling of interlobar arteries.

equipment will more readily define the optimal scanning plane. When the scan is not accurately centred on the lumen, spurious narrowing may be shown due to partial inclusion of the vessel side wall. Both arteries are often well defined, although bowel gas may present an insurmountable problem. Identification and differentiation from the renal vein depends upon showing the origin of the vessel from the aorta. This may be from the antero-lateral surface as in this case (Figs. 1 and 2) rather than from the more frequent lateral or postero-lateral position (Odman and Ranniger, 1968). The arterial lumen is normally echo-free. In the presence of thrombosis, the lumen shows a low-amplitude echo pattern. In the case under review, atheromatous changes affecting the renal artery were responsible for producing the thickening of the arterial wall seen on the echogram.

Although ultrasonography may suggest the diagnosis, arteriography remains the definitive investigation for demonstration of arterial stenosis or thrombosis.

This is the first case report of renal artery thrombosis diagnosed ultrasonically. We conclude that grey scale ultrasound can be used for the assessment of renal arteries in patients with hypertension.

ACKNOWLEDGMENTS

We wish to thank Dr. T. M. H. Chakera for his help and encouragement, Mrs. S. Mathie and Miss J. D'Mello for the typing of the manuscript, and Dr. P. Hurst for allowing us to use this case for publication.

REFERENCES

DUNNICK, N. R., SCHUETTE, W. H. and SHAWKER, T. H., 1979. Ultrasonic demonstration of thrombus in the common carotid artery. *American Journal of Roentgenology*, *133*, 544–545.

MERRITT, C. R. B., 1979. Ultrasonographic demonstration of portal vein thrombosis. *Radiology*, *133*, 425–427.

ODMAN, P. and RANNIGER, K., 1968. The location of the renal arteries. An angiographic and post-mortem study. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *104*, 283–288.

SCHULTZE, K., BENZE, U. F., SCHMITT, H. E. and MEUDT, R., 1977. Sonographic appearance of thrombosis of the inferior vena cava in renal tumours. *Fortschritte auf der Gebiete der Roentgenstrahlen und der Nuklearmedizin*, *126*, 231–235.

WHALEN, J. P., 1979. Radiology of the abdomen—impact of new imaging methods. *American Journal of Roentgenology*, *133*, 587–618.

1981, *British Journal of Radiology*, *54*, 353–355 APRIL 1981

Case reports

The role of ^{131}I-19-iodocholesterol scintigraphy and ultrasonography in the localization of a poorly vascularized phaeochromocytoma

By L. Troncone, M.D., P. G. Falappa, M.D., A. Cavallaro, M.D. and G. Netri, M.D.

Institutes of Nuclear Medicine, Radiology and Surgery of the Catholic University of Sacred Heart, Rome, Italy

(*Received December 1979 and in revised form June 1980*)

Cases have been reported in which phaeochromocytomas have been identified by adrenal gland scintigraphy with ^{131}I-19-iodocholesterol (or other steroid analogues) as well as by ultrasound (Sturman *et al.*, 1974; Helber *et al.*, 1975; Troncone *et al.*, 1977; Sample, 1978; Thrall *et al.*, 1978; Chatal *et al.*, 1979). However the role of these techniques, and in particular of adrenal imaging, in the localization of medullary tumours is still far from established.

The case reported here, concerning a patient with a surgically proven adrenal phaeochromocytoma, further supports the value of the radioisotopic procedure and the ultrasound studies in this field. In fact they succeeded in lateralizing correctly the tumour which was not visualized by selective arteriography, because of its minimal vascularity.

CASE REPORT

A 36-year-old male was admitted to the University Hospital in May 1978 with a 20-month history of paroxysmal hypertension. He complained of sudden attacks of headache, weakness, vomiting, diaphoresis and tachycardia. On admission, his blood pressure was 260/130 mmHg and his heart rate was 130 per minute.

Initially these crises recurred at intervals of three to four weeks; three months prior to admission, they became more frequent (once a day) and more severe.

On examination, no significant physical abnormalities were found. During normotensive periods, his blood pressure was 120/80 mmHg; heart rate 80 per minute. His weight was 75 kg.

The relevant laboratory findings were as follows: haematocrit 50%; RBC 6460000; WBC 17400; platelets 340000. Blood glucose level 110 mg/100 ml. Urinary catecholamins were higher than normal (Norepinephrine 1160 μg/24 h; VMA (Vanillyl Mandelic Acid) 33.8 mg/24 h). 17-Ketogenic steroids were increased also (33 mg/24 h)).

The chest radiograph was normal.

Paroxysmal transient subepicardial ischaemia was observed on the ECG as well as an increase of blood glucose (220 mg/100 ml), total bilirubin (3 mg/100 ml) and azotaemia (72 mg/100 ml).

The response with phentolamine test (Rogitin) was positive, producing a precipitous fall in blood pressure from 240/140 to 140/90 mmHg.

Because a phaeochromocytoma was suspected, treatment with oral phenoxybenzamine (Dibenzyline) (30–40 mg daily) was carried out for a period of three weeks in order to prevent hypertensive crises and in preparation for surgery.

Urography with tomography was carried out in an attempt to localize the tumour but no abnormalities were demonstrated. Aortography and selective renal arteriography were also inconclusive. Angiograms showed only some irregularities of the small left adrenal vessels, but they did not provide convincing evidence of the presence of a tumour (Fig. 1).

Adrenal gland scintigraphy was carried out using ^{131}I-19-iodocholesterol according to the method previously published (Troncone *et al.*, 1975). Photoscans were obtained two to ten days after an intravenous injection of 55.5 MBq (1.5 mCi) of radioiodocholesterol* using potassium perchlorate as a thyroid blocking agent. Kidney visualization was also performed (after 74 MBq (2 mCi) of ^{99}Tc^{m}-DMSA intravenously) in order to obtain a scintigraphic representation of the adrenal and kidney outlines simultaneously.

On the rectilinear photoscan the right adrenal appears normal in shape and activity distribution and it is placed, normally, on top of the upper renal pole. On the contrary, the left gland was poorly visualized and distorted with irregular and decreased activity, mainly in its lower half. Alterations of the adrenal gland were better imaged on the simultaneous representation of the adrenal and kidney outlines (Fig. 2), whereby distortion of the upper renal pole was also noted. These findings appeared suggestive of the presence of a left-sided tumour.

The suspicion was confirmed by ultrasound: the sonogram showed good evidence of a solid mass approximately 6 cm in diameter, causing compression of the left kidney (Fig. 3).

Left selective phlebography was diagnostic (Fig. 4) showing a non-vascular tumour in the inferior half of the adrenal gland.

At surgery a phaeochromocytoma, measuring 6.2 × 5 cm in diameter, was removed from the left adrenal gland (Fig. 5).

Post-operatively, urinary catecholamines were in the normal range and blood pressure returned to normal (120/80 mmHg).

DISCUSSION

Radiological procedures like the angiographic ones are proving to be the techniques of choice in the localization of medullary tumours. However, hazards and complications (hypertensive crises, extravasation, haemorrhagic adrenal necrosis, etc.), as well as reports of fatalities, resulted in a certain reluctance to perform these contrast procedures in patients with phaeochromocytoma (Rossi *et al.*, 1968; Eagan and Page, 1971; Sutton, 1975). Besides, it is well known that angiographic methods, even of the best quality, can fail to localize a proportion of phaeochromocytomas: for instance when an associated renal arterial stenosis exists, in a non-vascular or poorly vascularized tumour, or in multiple or ectopic phaeochromocytomas (Sutton, 1975).

The case we are dealing with plainly belongs to the last class because neither a good quality aortogram nor selective arteriography succeeded in providing

---

*^{131}I-19-iodocholesterol was supplied by Cis-Cea-Sorin, Saluggia, Italy.

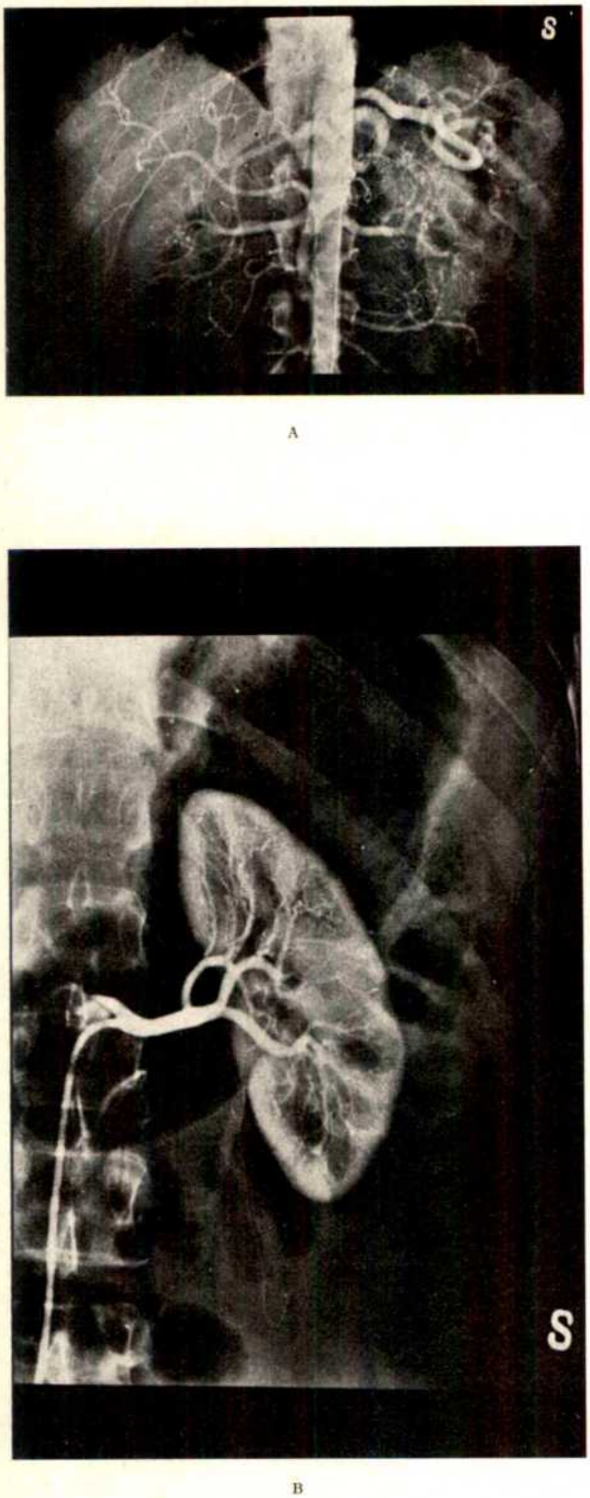


FIG. 1.

Abdominal aortography (A) and selective renal arteriography (B) do not provide convincing evidence of the presence of the tumour.

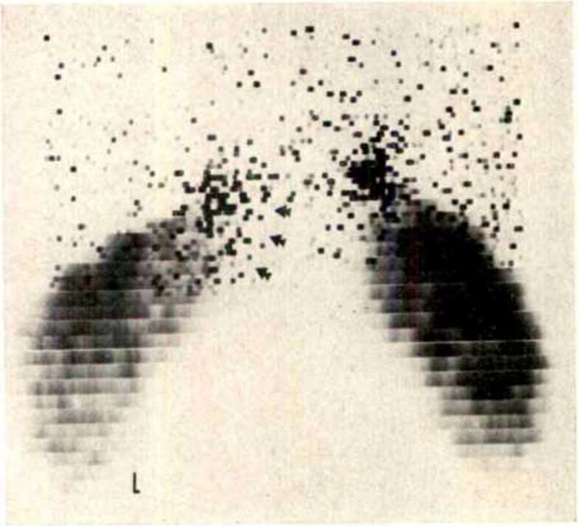


FIG. 2.

Adrenal scan (posterior view; representation of both the adrenals and kidney simultaneously). The left adrenal appears smaller than the right, poorly and irregularly active mainly at its lower border.

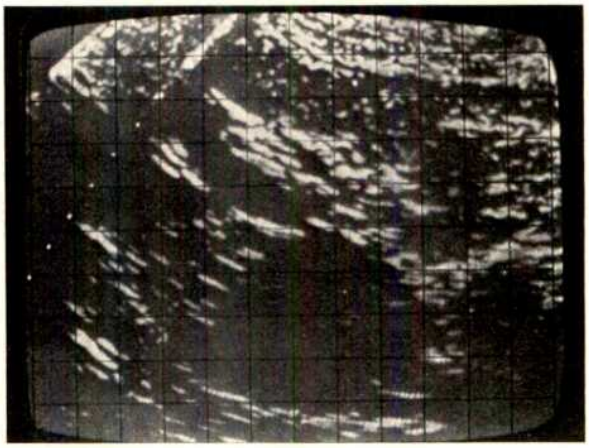


FIG. 3.

Ultrasound. Prone longitudinal B scan demonstrating normal left kidney and anteriorly, a round solid lesion, 5–6 cm in diameter, separated from it (left: head; right: feet).

convincing evidence of the presence of the tumour, owing to its minimal vascularity. As expected, selective phlebography visualized the tumour mass in the left adrenal gland, but this procedure was performed because of the suggestive evidence on scintigraphy and ultrasound.

With reference to ^{131}I-19-iodocholesterol scintigraphy, as reported elsewhere (Sturman *et al.*, 1974; Troncone *et al.*, 1977), this method (even though radioiodocholesterol is not taken up by the medullary tissue) allows one to localize medullary

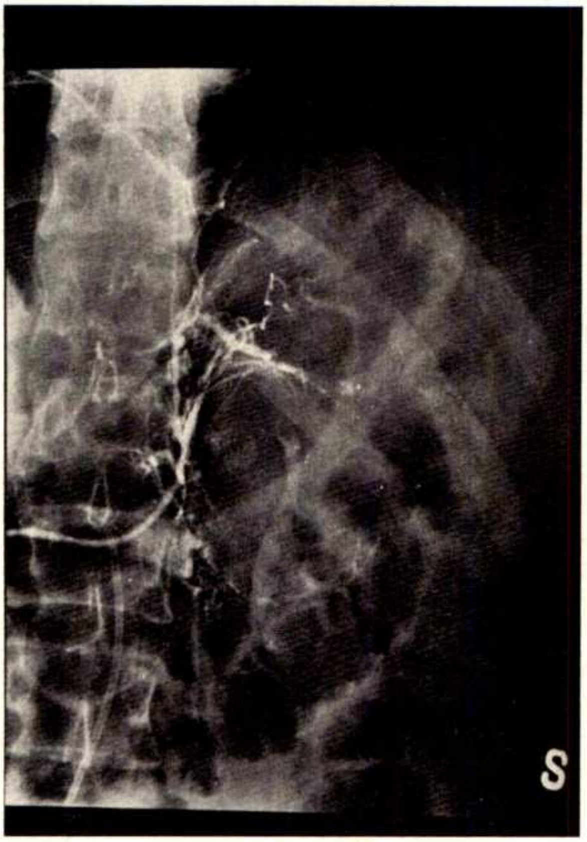


FIG. 4.
Left adrenal phlebography performed after the scintigraphic abnormalities were detected, shows a roundish filling defect superimposed on the kidney.

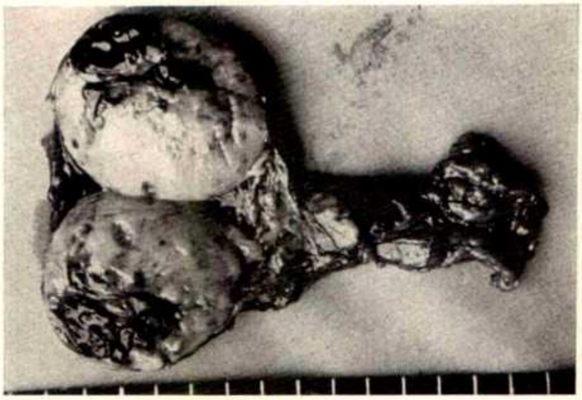


FIG. 5.
Bisected surgical specimen showing the phaeochromocytoma (6.2×5 cm in diameter).

tumours indirectly, through alterations which have been produced by the tumour itself in the adrenal cortical tissue. Distortion, decreased and irregular distribution of activity and notching of the adrenal cortical gland were the factors that allowed identification of the tumour. In the case presented ultrasound studies were also diagnostic. At present, this technique is scarcely used in the localization of adrenal gland tumours. It deserves much more interest and further application to establish its diagnostic value (Sample, 1978; Chatal *et al.*, 1979).

Computed tomography (CT) has also been reported to detect, with a high degree of accuracy, adrenal abnormalities (Dunnick *et al.*, 1979). In this study CT was not taken into consideration because both scintigraphy and ultrasonography had already resulted in a pathological diagnosis.

Adrenal scintigraphy, and above all, ultrasound, without doubt, are safer than angiography. Therefore in the diagnostic strategy for the localization of medullary tumours these techniques have to be regarded as the methods to be used before angiographic studies are undertaken, thus avoiding the latter or orientating and guiding them.

Studies to assess the relative role of the non-invasive procedures are in progress.

REFERENCES

CHATAL, J. F., VASSEUR, F., TALMANT, C., GROLLEAU, B., LUCAS, J. and CHARBONNEL, B., 1979. L'échotomographie et la scintigraphie au radiocholesterol pour le diagnostic topographique d'un phéochromocytome. *Nouvelle Presse Médicale*, *8*, 2673–2676.

DUNNICK, N. R., SCHANER, E. G., DOPPMAN, J. L., STROTT, C. A., GILL, J. R. and JAVADPOUR, N., 1979. Computed tomography in adrenal tumours. *American Journal of Roentgenology*, *132*, 43–46.

EAGAN, R. T. and PAGE, M. I., 1971. Adrenal insufficiency following bilateral adrenal venography. *Journal of the American Medical Association*, *215*, 115–116.

HELBER, A., DVORAK, K., WINKELMANN, W., MEURER, K. A., WURZ, H. and DICKMANS, A., 1975. 131 I-Cholesterin-Szintigraphie der Nebennieren. Erfahrungen bei verschiedenen Nebennierenerkrankungen, insbesondere einseitigen Nebennierentumoren. *Deutsche medizinische Wochenschrift*, *100*, 2524–2527.

ROSSI, P., YOUNG, I. S. and PANKE, W. F., 1968. Technique usefullness and hazards of arteriography in phaeochromocytomas. *Journal of the American Medical Association*, *205*, 547–573.

SAMPLE, W. F., 1978. Adrenal ultrasonography. *Radiology*, *127*, 461–466.

STURMAN, M. F., MOSES, D. C., BEIERWALTES, W. H., HARRISON, T. S., ICE, R. D. and DORR, R. P., 1974. Radiocholesterol adrenal images for the localization of phaeochromocytoma. *Surgery, Gynecology and Obstetrics*, *138*, 177–180.

SUTTON, D., 1975. The radiological diagnosis of adrenal tumours. *British Journal of Radiology*, *48*, 237–258.

THRALL, J. H., FREITAS, J. E. and BEIERWALTES, W. H., 1978. Adrenal scintigraphy. *Seminars in Nuclear Medicine*, *8*, 23–41.

TRONCONE, L., SALVO, D., VINCENZONI, M. and BARBARINO, A., 1975. Adrenal gland scintigraphy. A preliminary remark on a new radioisotopic technique. *Acta medica romana*, *5/6*, 128–139.

TRONCONE, L., FALAPPA, P. G., FOCACCI, C. and GALLI, G., 1977. ^{131}I-19-iodocholesterol scintigraphy for the localization of medullary tumours. *Journal of Nuclear Medicine and Allied Sciences*, *21*, 159–164.

1981, *British Journal of Radiology*, 54, 356–358

Technical notes

A hybrid real time/B scan ultrasonic system. Implications for clinical practice based on a two-year experience

By S. R. Wild, M.B., Ch.B., F.R.C.R., W. A. Copland, F.R.C.S.E., F.R.C.R.
Department of Radiodiagnosis, Western General Hospital, Edinburgh
and W. N. McDicken, B.Sc., Ph.D.
Department of Medical Physics and Medical Engineering, Royal Infirmary, Edinburgh

(Received September 1980)

As a result of recent technical advances in ultrasonic equipment, image quality has rapidly improved with important consequences. Less expertise is now required to produce good pictures and the scope of the modality has broadened. Accuracy rates have improved in the detection of smaller lesions paralleling increased confidence in defining normal anatomy and subtle changes in the parenchyma of solid organs.

The result in most departments has been an unprecedented increase in demand for ultrasonic examinations. Contrary to North American practice, the bulk of scanning in the UK, apart from obstetric work, is carried out by medically qualified personnel, usually radiologists, to whom this new situation has posed serious problems. Ultrasound in common with other new imaging techniques is introducing yet more work into a speciality where establishment is already considerably under strength, both at consultant level and throughout the training grades.

It was decided to make a retrospective assessment of how successful attempts have been to meet this problem in a busy ultrasound unit within an X-ray department. Until 1975 the ultrasound work of the department was largely confined to obstetric practice and carried out on a single bi-stable display B scan unit (Nuclear Enterprises 4102). This was upgraded with an analogue scan converter in 1976. The new grey-scale display facilitated the examination of solid abdominal organs and consequently the demand for non-obstetric work rose rapidly (Table I). A second grey-scale B scan unit was subsequently commissioned (Nuclear Enterprises 4201) in a separate adjacent room, thus allowing obstetric and non-obstetric examinations to proceed simultaneously. The relatively fast patient throughput in the obstetric room was able to proceed unhindered while the radiologist working in the non-obstetric area was always present to supervise any difficult problems encountered by the radiographic staff. In addition, breakdown of one unit no longer brought departmental work to a standstill. Despite this, it was anticipated that, allowing a minimum of half an hour for each non-obstetric patient, and running the equipment for ten sessions per week, by 1978 both machine and operator time would be fully utilized.

The theoretical advantages offered by real-time ultrasound were investigated and a number of systems evaluated, mainly of the mobile linear array type or linear arrays which could be added to standard B scan equipment.

Experience with these linear array systems was disappointing on a number of counts. Good skin contact was an inherent problem. Picture quality was generally poor and there was an almost universal lack of "frame freeze" facilities at that time. Where the latter were provided there was always a disappointing loss of information in the static image. In essence, none of the linear array systems evaluated gave information comparable to a B scanner (Health Equipment Information No. 81, 1979).

At the same time a 3.5 MHz four element mechanical rotating sector scanner was interfaced with the B scan unit. This hybrid system produced impressive results. The quality of both the real-time images and the static pictures produced using the electronics and display of the B scanner were superior to any from existing linear arrays. The size and shape of the head of the mechanical rotating transducer were well suited to interrogate the organs of the upper abdomen, the 90° sector being ideal for producing scans with the same orientation as the

TABLE I

NUMBERS OF NON-OBSTETRIC ULTRASONIC EXAMINATIONS CARRIED OUT BETWEEN 1976 AND 1979

Year	Number of examinations
1976	276
1977	794
1978	1322
1979	2010

single sweep of the B scan transducer under the costal margin (Bow *et al.*, 1979).

A point of particular significance is the method of producing static images using the mechanical rotating transducer in conjunction with a high resolution scan converter. The scan plane of interest is quickly identified by the operator using the scanning head in the conventional real-time mode. By the activation of a pedal switch the rotation is stopped, and one of the four transducers performs a single 90° sector scan in approximately one second, collecting and storing 750 lines of echo information in the scan converter and subsequently presenting a high line density image on the display. The line density compares well with a B scan image and is five times higher than that of the real-time image (Figs. 1 and 2). Another factor contributing to the comparability of frozen real-time and B scan images is that the same type of transducer is used. Single crystal focused transducers are well proven in the production of high quality images. Slow frame freeze images can be produced both by mechanically rotating transducers and by electronically phased array scanners. This facility is not found at present in linear array systems.

The hybrid system (B scanner with scan converter and add-on mechanically rotating transducer) has now been used during a period of nearly two years and over 3000 non-obstetric cases have been studied

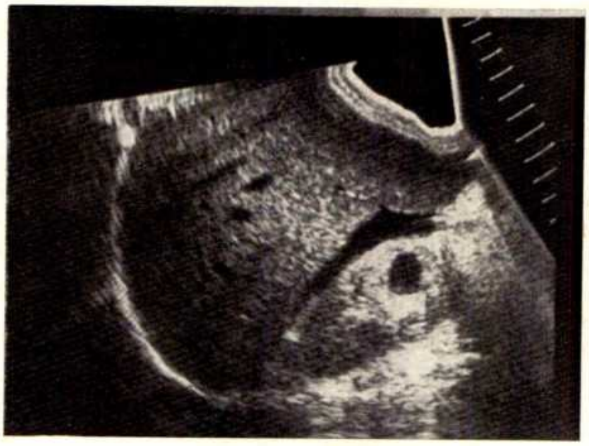


FIG. 1A.

Single pass B scan. Longitudinal section through right lobe of liver showing small amount of free fluid between liver and right kidney and 2 cm cyst in the right kidney. 13 mm 3.5 MHz transducer with medium internal focusing.

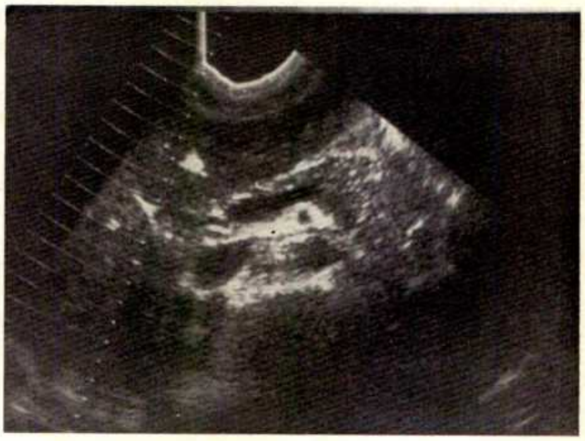


FIG. 2A.

Single pass B scan. Transverse section through the upper abdomen showing the pancreas and related anatomy. 13 mm 3.5 MHz transducer with medium internal focusing.

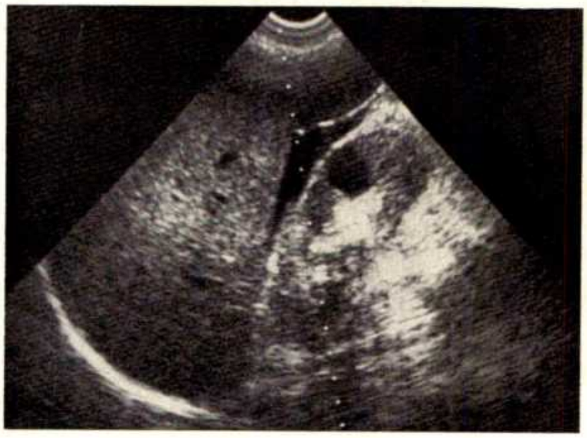


FIG. 1B.

Same patient scanned with 3.5 MHz mechanical rotating transducer, the static image being produced by a single sweep "frame freeze".

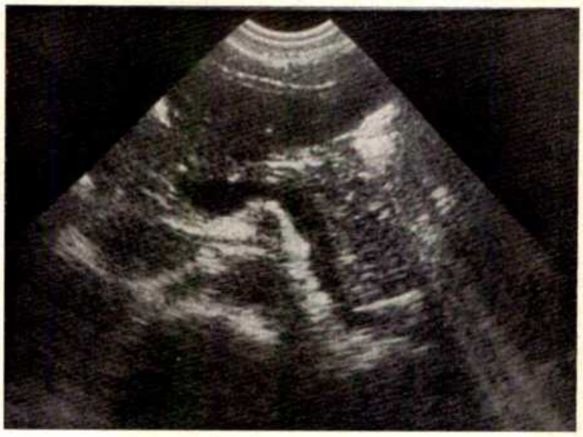


FIG. 2B.

Same patient. Single sweep "frame freeze" from the mechanical rotating transducer. Comparable transverse section through the pancreas.

in addition to a large obstetric population. The real-time element of the system affords rapid examination of the abdominal organs, thus enabling the operator to screen the whole upper abdomen even when only one specific organ examination has been requested. The chance of identifying pathology is therefore increased. Organs may be interrogated from positions and angles not possible with the more rigid B scanner arm. The position and alignment of organs such as the gall bladder and pancreas, the courses of blood vessels and the biliary tree are readily located allowing more detailed examination with the B scanner if required. Small calculi within the gall bladder are much less likely to be overlooked than if the B scanner is used alone.

Examination times have been reduced by factors of between two and five times. In a review of 100 gall bladders recently studied, average scanning time was four minutes and in no case was it necessary to resort to B scanning.

During the last 12 months the throughput of patients on the hybrid system as compared with numbers before the addition of the mechanical rotating transducer has increased by more than 50%, and at the present time in over 80% of cases all the information required may be obtained by exclusive use of the mechanical rotating transducer with "frame freeze" imaging. The B scan element of the system is now reserved for patients in whom compound scanning for a large field of view is required or where the examination dictates the use of either a higher or lower ultrasonic frequency. An important practical point to note is that as the production of the real-time moving image is independent of the scan converter, failure of this component need not stop examinations being carried out although no static images can be made. Conversely, if the mechanical rotating transducer fails, the operator can revert to conventional B scanning.

An additional advantage offered by the real-time element of the system is the ability to detect and record (on video tape) the movement of structures, for example vascular and respiratory pulsation, gall bladder contraction and gastric peristalsis.

The limitations of the hybrid system during this extended period of use have been few. It was expected that there might be problems with the mechanical operation of the sector scanner but in practice this has been remarkably reliable. Unfortunately, inherent in the construction of the present probe is loss of detail in the first 2 cm range, which poses a problem when superficial organs such as the thyroid are studied and also in the examination of very small babies. The lack of mobility of the whole system in our experience has not proved to be a serious disadvantage in clinical practice.

All the foregoing comments apply equally to our obstetric work. Examination time is significantly reduced. Fetal heart movement may be readily detected and recorded from between seven and eight weeks of gestational age. Biparietal measurements are more easily made even when the baby is lying in an unusual position and twin pregnancies are rapidly and confidently diagnosed at all stages of pregnancy. The high quality frame-frozen image improves consistency in measuring crown–rump lengths in early pregnancy. The ability to display and record the anatomy of the fetal heart augurs well for the future in the area of ante-natal detection of certain types of congenital heart disease.

This concept of hybridization of ultrasound systems offers considerable potential for the future by allowing additional facilities to be interfaced with a basic package, central to which is high quality and high capacity electronics. This lends itself to the addition of real-time PPI (Plan Position Indicator) scanning, biopsy probes and possibly modules dedicated to scanning particular areas such as the eye. At the other end of the system the output signal from the scan converter may be used in a variety of different image recording options and is also available for electronic processing.

The extended use of a hybrid ultrasound package has modified non-obstetric and obstetric practice with respect to both the quality and the quantity of examinations with a significant increase in departmental work capacity. This type of system represents a major technical development and provides a powerful diagnostic tool in the field of non-invasive medical imaging.

REFERENCES

Bow, C. R., McDicken, W. N., Anderson, T. Scorgie, R. E. and Muir, A. L., 1979. A rotating transducer real-time scanner for ultrasonic examination of the heart and abdomen. *British Journal of Radiology*, *52*, 29–33.

Health Equipment Information No. 81, 1979. Evaluation of Real Time Ultrasonic Scanner (First Report) (Scottish Home and Health Department).

1981, *British Journal of Radiology*, *54*, 359–360 APRIL 1981

Technical notes

Measurement of chest-wall thickness using a simulator

By C. F. Westermann and G. Kok

Departments of Clinical Physics and Radiation Oncology, Westeinde Hospital, The Hague, The Netherlands

(*Received September 1980 and in revised form November 1980*)

In the radiotherapy of breast cancer the position of the inner chest-wall is very important, as it is the border line between the target area and the adjoining normal lung tissue that must be spared. Determination of this position by computerized tomography is not possible for us because the aperture size of a CT body-scanner is too small for the patient in the treatment position. The upper half of the patient's body is tilted in such a way that the sternum reaches a horizontal position whilst the upper arm of the patient is lifted upwards as high as possible to get it out of the beam. The patient holds a handle that is fixed to a tilting device on the table top. A solution to this localization problem may be found using a simple scanning technique with a normal simulator.

METHOD

The control desk of the simulator must be equipped with a digital read-out of the gantry angle and the x-, y- and z-positions of the table top. This feature did not form a part of the standard accessories of our Philips simulator type XK 4104, but in co-operation with the manufacturer a handy read-out system was produced which has proved to be very useful for other purposes too.

To start the localization procedure the patient is brought into the treatment position on the simulator and body outlines are drawn by conventional means in a number of parallel planes of interest. A reference point is marked both on the skin of the sternum in the central plane and on the drawing of the outline. Then with the gantry in the vertical position this point on the patient's skin is brought to the isocentre by moving the table top, and the horizontal and vertical positions of the table top ($x_{\text{ref}}, y_{\text{ref}}$) are noted (Fig. 1A). The gantry is then set horizontally and the table top is moved upwards under fluoroscopy until the frontal side of the inner chest-wall is at isocentric height. Now the vertical position of the table top (y_{F}) is noted (Fig. 1B).

The gantry is then rotated over 10° to an oblique angle ϕ and under fluoroscopy the treatment table is shifted horizontally in such a way that the central ray is at a tangent to the inner chest-wall. Then the horizontal position of the table top (x_{ϕ}) is noted. Again the gantry is rotated over 10° to another angle ϕ and in the same way a new value of x_{ϕ} is found. This procedure is repeated until the gantry has scanned an angle of 110° from the horizontal position with regular intervals of 10°.

Figure 2A shows the position of the patient and the simulator in a typical case and Fig. 2B presents a radiograph, made in this position, showing the central axis crosswires of the beam aligned tangentially with the inner chest-wall. This procedure can be repeated for other planes after shifting the table

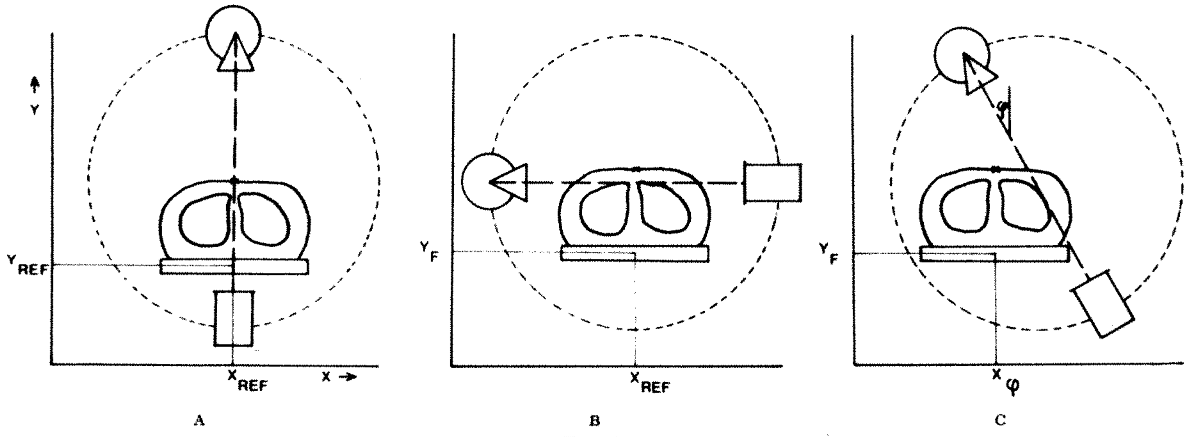


FIG. 1.

(A) The reference point (cross) is placed at the isocentre.

(B) The frontal side of the inner chest-wall is determined.

(C) The inner chest-wall is scanned at different angles, ϕ.

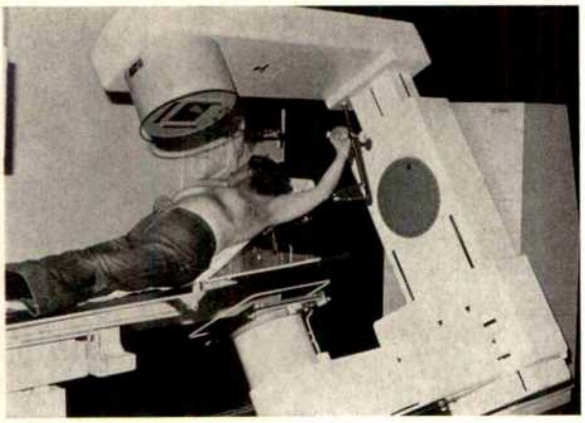


FIG. 2A.

Position of the patient and the simulator, in a typical case, during the scanning procedure. The gantry angle ϕ is 30°.

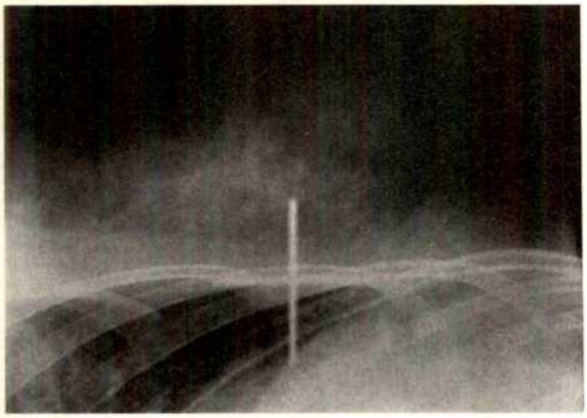


FIG. 2B.

Radiograph, made in the position of Fig. 2A, showing the central-axis crosswires of the beam aligned tangentially with the inner chest-wall.

top parallel to the gantry rotation axis (z-direction). If by that time the position of the patient on the table top has slightly altered, a new reference point must be chosen. One may scan in this way three

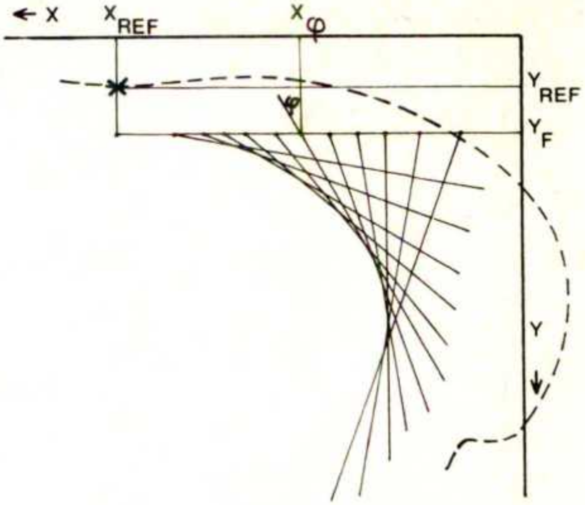


FIG. 3.

Reconstruction of the inner chest-wall by tangential lines at an angle φ through a point x_ϕ, y_F. The broken line represents the body outline.

outlines of the thorax in 15 to 20 minutes. A pre-printed form facilitates quick recording of the data.

For reconstruction one uses a piece of graph paper with inverted x- and y-axes (Fig. 3). The points (x_{ref}, y_{ref}) and (x_{ref}, y_F) are marked and lines at an angle ϕ are drawn through the points (x_ϕ, y_F). The inner chest-wall can be found as a curve that is tangential to these lines. With the aid of the reference point this curve can be positioned in the drawing of the body outline.

To get an indication of the accuracy, we have measured outlines of a plaster dummy patient with our normal outline measuring device and with the simulator method. The differences were within 3 mm, except where the contour was concave. Fortunately the lung contour does not show concave outlines in the area of interest.

This method has now been incorporated for three years in our routine localization procedure of patients who were to be irradiated for breast cancer. It is considered to be very useful.

1981, *British Journal of Radiology*, 54, 361–362 APRIL 1981

Short communications

Radiation survival of glutathione-deficient human fibroblasts in culture

By P. J. Deschavanne, D.Sc., E. P. Malaise, M.D., Ph.D.

Laboratoire de Radiobiologie Cellulaire, Institut Gustave-Roussy, 94800 Villejuif, France

and L. Révèsz, M.D., Ph.D.

Institutet För Tumörbiologi II, Karolinska Institutet, 104 01 Stockholm 60, Sweden

(*Received July 1980 and in revised form November 1980*)

Observations on a correlation between radiation survival and the cellular level of non-protein bound sulphydryl groups (NPSH) have been interpreted as indicating that these substances may be of particular importance in determining the intrinsic radiosensitivity of cells (Bruce *et al.*, 1969; Ohara and Terasima, 1969; Révèsz *et al.*, 1963; Sinclair, 1969). In considering the radioprotective effect of different aminothiols, those occurring naturally in the cells may act as natural radioprotectors. In mammalian cells, glutathione constitutes the overwhelming part, if not the entire NPSH content (Modig and Révèsz, 1967; Scaife, 1966). The main protective mechanisms were considered to be the scavenging of radiation-induced radicals as well as the restoring of radiation-damaged molecules by hydrogen donation in competition with other molecules which would fix the damage (Alexander and Charlesby, 1955; Chapman *et al.*, 1973). Glutathione has also been shown to be a coenzyme in the synthesis of deoxyribonucleotides in *E. coli* (Holmgren, 1976; 1979) and therefore could be involved in DNA repair.

Experimental studies on the role of NPSH in determining radiation survival, by using cells depleted in NPSH after treatment with SH-reactive compounds such as N-ethylmaleimide (NEM) or diamide (Chapman *et al.*, 1973), have the disadvantage that these compounds can have unspecific side effects possibly influencing survival. No such disadvantage is to be expected by using cell lines with a genetically defined deficiency in glutathione-synthetase (Larsson *et al.*, 1976). This deficiency results in a decreased concentration of NPSH (around 50% of normal) consisting mainly of glutamine-cysteine and cysteine-glycine (Edgren, personal communication), and with glutathione present only in a small amount (less than 5% of normal) (Révèsz *et al.*, 1979).

In our radiation survival tests, we used fibroblasts derived from subcutaneous biopsy material from an individual (V.P.) suffering from an inborn error of glutathione synthetase activity (Larsson *et al.*, 1976). Fibroblast cultures derived from V.P.'s clinically healthy brother (G.P.) (Larsson *et al.*, 1976), without any known metabolic error, were used as control. Cells grew as a monolayer culture in Eagle's Minimum Essential Medium (Earle's salts) supplemented with 15% fetal calf serum and antibiotics. Cells in 16th to 25th (V.P.) and 13th to 15th (G.P.) generations were used for the experiments.

We adopted a method previously described (Deschavanne *et al.*, 1980) to determine the radiosensitivity of the cells, using maintenance of clonogenic capacity as an end point. As the plating efficiency depended on the cell density, a variable number of heavily irradiated (30 Gy) feeder cells were added to the cell population to be tested for survival, so that the final cell density was, in all cases, 4×10^3 cells per cm^2. Irradiations were made with ^{137}Cs γ rays at a dose rate of 0.8 Gy per min.

The mean percentage plating efficiency, even in the presence of heavily irradiated cells, was low for both V.P (13.2 ± 1.3) and G.P. cells (8.3 ± 1.3).

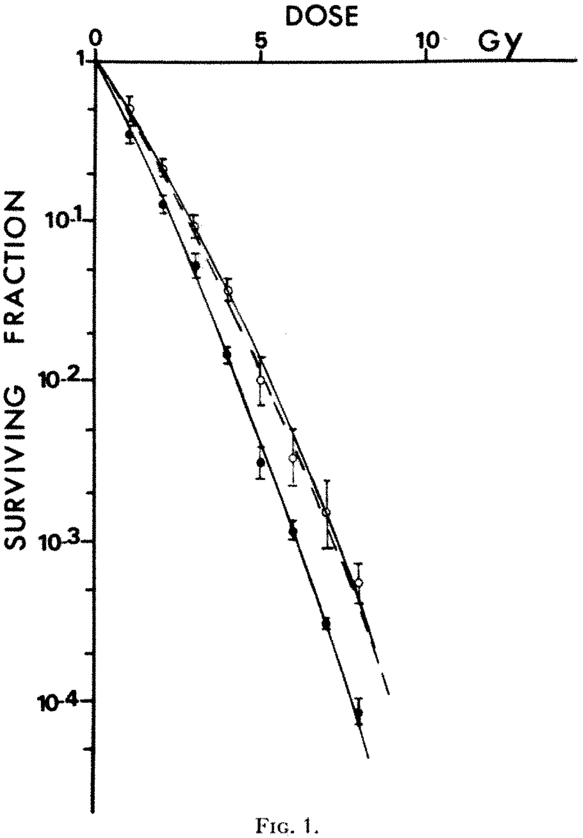


FIG. 1.

Radiation survival curves of fibroblasts derived from an individual (V.P.) suffering from an inborn error of glutathione synthetase activity, and his healthy brother (G.P.) with no known metabolic error. Points and vertical bars indicate the mean and SE calculated from 4–5 replicate determinations. Solid lines were calculated adopting the linear-quadratic survival model with $\alpha = 9.73 \pm 0.59 \times 10^1 \mathrm{Gy}^{-1}$ and $\beta = 2.58 \pm 0.9 \times 10^2 \mathrm{Gy}^{-2}$ for V.P. and $\alpha = 7.59 \pm 0.69 \times 10^1 \mathrm{Gy}^{-1}$ and $\beta = 2.48 \pm 1.05 \times 10^2 \mathrm{Gy}^{-2}$ for G.P. For comparison, the survival curve of another untransformed human fibroblast HF 19 ($\alpha = 7.38 \times 10\ \mathrm{Gy}^{-1}$ and $\beta = 2.93 \times 10^2 \mathrm{Gy}^{-2}$), determined in an identical way, is also indicated by the dashed line.

●– – –● V.P.; ○– – –○ G.P.; – – – – – – HF 19.

Supported in part by La Ligue Nationale Contre le Cancer (Comité des Hauts-de-Seine) and by contract No. 82070 B00-D20 from Electricité de France.

Reprint requests to P. Deschavanne.

1981, *British Journal of Radiology*, *54*, 362–363

In comparison to G.P., the survival of V.P. was decreased at all radiation doses tested (Fig. 1), indicating a dose-modifying factor of 1.26 and 1.13 at survival levels of 10^{-1} and 10^{-2} respectively. V.P. appears to be more sensitive than a great number of fibroblastic cell lines studied so far (Deschavanne *et al.*, 1980). When the survival curves are fitted to the linear quadratic model (Fertil *et al.*, 1980; Kellerer and Rossi, 1972), only a slight difference can be seen in the quadratic component of V.P. and G.P., and the main difference appears to be in the linear component which is larger in the case of V.P. than G.P. This suggests that the lethal events expressed by the two parameters are influenced differently by a decreased NPSH level and/or glutathione deficiency. The parameters for G.P. are similar to those found earlier with the same method for another untransformed fibroblast culture (HF 19) which had a plating efficiency almost seven times greater (Deschavanne *et al.*, 1980).

The increased sensitivity of V.P. can be attributed to a decreased intrinsic protection due either to the decreased cellular NPSH concentration in general and/or to the almost total lack of glutathione in particular. The particular importance of glutathione as an intrinsic protector, as contrasted to other naturally occurring aminothiols, is strongly supported by recent observations that oxygen does not enhance DNA strand breakage in V.P. cells (Edgren *et al.*, 1980). In considering the competition theory for the oxygen effect (Alexander and Charlesby, 1955), the lack of this effect despite the presence of aminothiols other than glutathione indicates that glutathione has a particular capacity to compete with oxygen and to repair radiation-induced radicals. Other naturally occurring aminothiols appear to be much less effective, or even totally ineffective, as competitors, though they may still be efficient as protectors in some other respect, *e.g.* as scavengers. Survival curves of anoxically irradiated glutathione deficient cells, and the use of different (artificial) aminothiols with known protective effect, can be expected to throw further light upon the possible uniqueness of glutathione as an intrinsic protector.

REFERENCES

Alexander, P. and Charlesby, A., 1955. Physio-chemical methods of protection against ionizing radiation. In *Radiobiology Symposium, Liège, 1954*, Ed. Z. M. Bacq and P. Alexander, (Butterworth, London) p. 49.

Bruce, A. K., Sansone, P. A. and MacVittie, T. J., 1969. Radioresistance of bacteria as a function of p-hydroxymercuribenzoate binding. *Radiation Research*, *38*, 95–108.

Chapman, J. D., Reuvers, A. P., Borsa, J. and Greenstock, C. L., 1973. Chemical protection and radiosensitization of mammalian cells growing *in vitro*. *Radiation Research*, *56*, 291–306.

Deschavanne, P. J., Fertil, B., Lachet, B. and Malaise, E. P., 1980. Radiosensitivity and repair of radiation damage in human HF 19 fibroblasts. *International Journal of Radiation Biology*, *38*, 167–177.

Edgren, M., Larsson, A., Nilsson, K., Révèsz, L. and Scott, O. C. A., 1980. Lack of oxygen-effect in glutathione-deficient human cells in culture. *International Journal of Radiation Biology*, *37*, 299–306.

Fertil, B., Deschavanne, P. J., Lachet, B. and Malaise, E. P., 1980. *In vitro* radiosensitivity of six human cell lines. A comparative study with different statistical models. *Radiation Research*, *82*, 297–309.

Holmgren, A., 1976. Hydrogen donor system for E. coli ribonucleoside-diphosphate reductase dependent upon glutathione. *Proceedings of the National Academy of Sciences*, USA, *73*, 2275–2279.

1979. Glutathione-dependent synthesis of deoxyribonucleotides. Characterization of the enzymatic mechanism of Escherichia coli glutaredoxin. *The Journal of Biological Chemistry*, *254*, 3672–3678.

Kellerer, A. M. and Rossi, H. H., 1972. The theory of dual radiation action. *Current Topics in Radiation Research Quarterly*, *8*, 85–158.

Larsson, A., Zetterström, R., Hörnell, H. and Porath, U., 1976. Erythrocyte glutathione synthetase in 5-oxoprolinuria: kinetic studies of the mutant enzyme and detection of heterozygotes. *Clinica Chemica Acta*, *73*, 19–23.

Modig, H, and Révèsz, L., 1967. Non-protein-sulphydryl and glutathione content of Ehrlich ascites tumour cells after treatment with the radioprotectors AET, cysteamine and glutathione. *International Journal of Radiation Biology*, *13*, 469–477.

Ohara, H. and Terasima, T., 1969. Variation of cellular sulphydryl content during cell cycle of HeLa cells and its correlation to cyclic changes of X-ray sensitivity. *Experimental Cell Research*, *58*, 182–185.

Révèsz, L., Bergstrand, H. and Modig, H., 1963. Intrinsic non-protein sulphydryl levels and cellular radiosensitivity. *Nature*, *198*, 1275–1277.

Révèsz, L., Edgren, M. and Larsson, A., 1979. Mechanism of radiosensitization by oxygen and misonidazole studied with glutathione deficient human fibroblasts in culture. In *Radiation Research. Proceedings of the sixth international congress of radiation research*. Ed. S. Okada, M. Imamura, T. Terasima and H. Yamaguchi (Toppan Printing Co. Ltd., Tokyo), pp. 862–866.

Scaife, J. F., 1966. An enzymatic evaluation of thiol radioprotectors. *Canadian Journal of Biochemistry*, *44*, 319–330.

Sinclair, W. K., 1969. Protection by cysteamine against lethal X-ray damage during the cell cycle of Chinese hamster cells. *Radiation Research*, *39*, 135–154.

Pulmonary metastases from differentiated thyroid carcinoma detected only by radionuclide imaging

By D. Casara, M.D., P. L. Zorat, M.D., B. Busnardo, M.D. and M. E. Girelli, M.D.

Thyroid Unit, General Hospital and School of Medicine, Padua, Italy

(*Received August 1980 and in revised form November 1980*)

Papillary thyroid carcinoma tends to metastasize to cervical lymph nodes while follicular carcinoma more usually produces haematogenous metastases particularly in the lung (Woolner *et al.*, 1961). We have observed 14 cases of lung metastases from differentiated thyroid carcinoma, detected only by ^{131}I scan, and the clinical findings are reported here.

Materials and Methods

The patients were seen in the thyroid unit of the General Hospital and School of Medicine of Padua. From 1962 to

---

Address for reprints: Dario Casara, M.D., Divisione di Radioterapia e Medicina Nucleare, Ospedale Civile, 35100 Padova, Italy.

TABLE I

CLINICAL FINDINGS IN PATIENTS WITH PULMONARY METASTASES DETECTED ONLY BY ^{131}I SCAN

Patient	Age (years)	Sex	Histological diagnosis	Location of metastases
T.I.	42	F	Follicular	—
S.B.	35	F	Pure papillary	Cerv. lymph. nodes
R.G.	27	F	Pure papillary	Cerv. lymph. nodes
C.E.	62	F	Follicular	Bones
Z.A.	57	F	Follicular	Cerv. lymph. nodes
Z.D.	46	M	Mixed pap. foll.	Cerv. lymph. nodes
F.R.	17	M	Pure papillary	Cerv. lymph. nodes
C.M.	30	F	Mixed pap. foll.	Cerv. lymph. nodes
F.ML.	45	F	Mixed pap. foll.	Cerv. lymph. nodes
C.F.	28	M	Follicular	Cerv. lymph. nodes
V.S.	40	M	Follicular	Cerv. lymph. nodes
Z.F.	12	M	Follicular	Cerv. lymph. nodes
C.A.	34	F	Follicular	—
R.C.	20	M	Pure papillary	—

1978 520 cases of differentiated thyroid carcinoma were studied; 290 were papillary and 230 were follicular carcinoma.

Criteria and histological classification were adopted in agreement with Beierwaltes *et al.* (1969) and Meissner *et al.* (1969).

The methods of treatment and follow-up were reported in previous publications (Busnardo *et al.*, 1976; 1977). During clinical staging and follow-up of 520 thyroid carcinomas, 14 cases of pulmonary metastases undetected röntgenographically were demonstrated by ^{131}I lung scan.

In our centre whole-body scanning is performed 48–72 h after oral administration of 185 MBq (5 mCi) of ^{131}I and after stopping T-3 for two weeks before administration of iodine.

Table I shows clinical findings in these patients. Seven cases were follicular, four pure papillary and three mixed papillary and follicular carcinomas. Age varied between 12 and 62 years (seven were less than 40 years of age). In three cases ^{131}I uptake was demonstrated only in the lungs, ten cases had metastases also in cervical lymphnodes and one also had metastases in bones (cranium and pelvis). In 12 cases pulmonary uptake was observed at the first diagnostic ^{131}I scan 6–8 weeks after thyroidectomy. In two cases pulmonary uptake was demonstrated after ^{131}I ablative therapy for remaining tissue after thyroidectomy. Therapeutic doses of ^{131}I were given at four to six month intervals until uptake in lungs or other metastases had disappeared. The therapeutic doses were calculated on the basis of iodine uptake and metastasis size (3.7–7.4 GBq, 100 to 200 mCi). Patients were maintained on T-3 suppressive treatment between the radioiodine therapy doses.

DISCUSSION

Life expectancy of patients with differentiated thyroid carcinoma is relatively long but metastatic spread reduces survival (Russell *et al.*, 1975). Early identification and treatment of metastases can improve survival (Leeper, 1973). Lungs are a frequent site of haematogenous metastases in thyroid carcinoma. Tumours in these sites are usually apparent on the chest radiograph. The demonstration of pulmonary metastases only by radionuclide imaging was first described in 1956 (Catz and Starr) and additional experience of the phenomenon was reviewed in 1973 (Bonte and McConnell) but probably many other cases have been seen in nuclear medicine centres. Pulmonary metastases undetected radiographically have also been observed in young patients and in cases of papillary carcinoma.

These considerations give further support to adopting a radical therapeutic regimen in differentiated thyroid carcinoma also in younger patients and in papillary carcinoma. Only total thyroidectomy allows the use of ^{131}I in early clinical staging and in early therapy. Furthermore these considerations are in agreement with a recent report (Mazzaferri *et al.*, 1977) which has shown that total thyroidectomy and ^{131}I therapy reduce both recurrence and mortality rate in papillary thyroid carcinoma.

REFERENCES

BEIERWALTES, W., DEGROOT, L. J., FEIND, C. R., KRISS, J. P., MEISSNER, W. A. and WERNER, S. C., 1969. Classification of thyroid disease. Report of the Committee on Nomenclature of the American Thyroid Association. *Journal of Clinical Endocrinology*, *29*, 860.

BONTE, F. J. and MCCONNELL, R. W., 1973. Pulmonary metastases from differentiated thyroid carcinoma demonstrable only by nuclear imaging. *Radiology*, *107*, 585–590.

BUSNARDO, B., VANGELISTA, R., GIRELLI, M. E., BUI, F. and LAZZI, C., 1976. TSH levels and TSH response to TRH as a guide to the replacement treatment of patients with thyroid carcinoma. *Journal of Clinical Endocrinology and Metabolism*, *42*, 901–906.

BUSNARDO, B., GIRELLI, M. E., CIMITAN, M., CASARA, D., BUI, F., LAZZI, C. and ARGENTI, G., 1977. Relationship between metastases of differentiated thyroid carcinoma and serum thyrotropin (TSH) levels. *Journal of Clinical Endocrinology and Metabolism*, *44*, 1193–1196.

CATZ, B. and STARR, P., 1956. Cancer of the thyroid with metastases to the lungs: condition shown by scintigram in absence of definitive X-ray findings. *Journal of the American Medical Association*, *160*, 1046–1047.

LEEPER, J., 1973. The effects of ^{131}I therapy on survival of patients with metastatic papillary or follicular thyroid carcinoma. *Journal of Clinical Endocrinology and Metabolism*, *36*, 1143.

MAZZAFERRI, E. L., YOUNG, R. L. and OERTEL, J. E., 1977. Papillary thyroid carcinoma: the impact of therapy in 576 patients. *Medicine*, *56*, 171–196.

MEISSNER, W. A. and WARREN, S., 1969. Tumors of the thyroid gland. *Atlas of tumor pathology*. Series II, fasc. 4. (Armed Forces Institute of Pathology, Washington, DC).

RUSSELL, M. A., GILBERT, E. F. and TAESCHKE, W. F., 1975. Prognostic features of thyroid cancer. *Cancer*, *36*, 553–559.

WOOLNER, L. B., BEARHRS, O. H., BLACK, B. M., MCCONAHEY, W. M. and KEATING, F. R., 1961. Classification and prognosis of thyroid carcinoma. *American Journal of Surgery*, *102*, 354–389.

1981, *British Journal of Radiology*, 54, 364

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Deceptive duodenal deformity

THE EDITOR—SIR,

I was interested in the report by Yoong and House (1980) describing the renal impression on the lateral margin of the duodenum. I too was puzzled by this when I first saw it (Fig. 1) but an injection of urographic contrast medium to opacify the kidney (Fig. 2) resolved the problem. This normal finding is also illustrated in Laufer (1979).

Yours, etc.,
I. BEGGS.

Department of Radiology,
University College Hospital,
Gower Street,
London WC1E 6AU.
(*Received December 1980*)

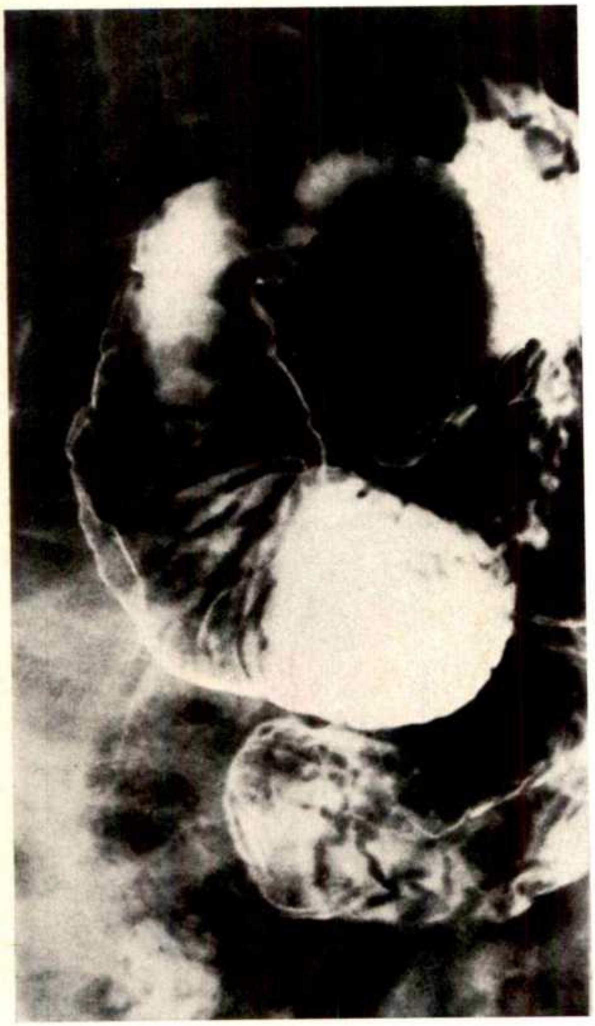


FIG. 1.

Hypotonic duodenogram: extrinsic impression on lateral margin of second part of duodenum.

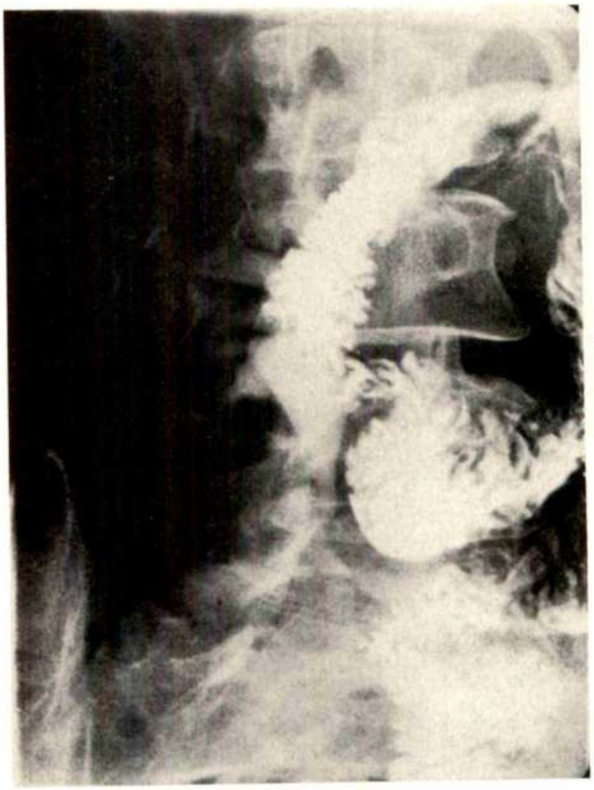


FIG. 2.

After injection of urographic contrast: demonstrating close relationship between renal pelvis and second part of duodenum.

REFERENCES

LAUFER, I. (ed), 1979. Double contrast gastro-intestinal radiology with endoscopic correlation (WB Saunders, Philadelphia/London/Toronto).

YOONG, P. and HOUSE, R., 1980. Deceptive duodenal deformity. *British Journal of Radiology*, *53*, 1012–1014.

Isolated dislocation of the pisiform

THE EDITOR—SIR,

I have read the article of Murali Sundaram *et al.* (1980) about a case of isolated dislocation of the pisiform. Since I have been interested in the functional X-ray anatomy of the pisiform and of the triquetro-pisiform joint for some years may I add some thoughts to the case mentioned above? Most anatomical textbooks state that the pisiform is firmly attached to the triquetrum with only minimal possibilities of moving. This is not true. I have made functional serial exposures of the wrist in order to test the physiological movements of the pisiform and in most cases the following movement components could be demonstrated: volar dislocation in flexion; distal movement in extension; proximal movement in flexion; rotation around an oblique horizontal axis. These phenomena could be explained on the evidence of arthrographic examinations. Loss of piso-triquetral parallelism occurs also under normal circumstances. Whether a dislocation actually occurs is questionable and I am not convinced by the X-ray pictures that in the case of Sundaram *et al.* there was really a dislocation of the pisiform. The radiologist must know the functional anatomy and the possibilities of movements under normal circumstances. Without this the diagnosis "dislocation of the pisiform" would be made perhaps more frequently than its true occurrence.

Yours, etc.,
A. LACZAY.

X-ray Department,
City Hospital,
Komló,
H-7301 Hungary.

(*Received November 1980*)

REFERENCES

SUNDARAM, M., SHIVELY, R., PATEL, B. and TAYOB, A., 1980. Isolated dislocation of the pisiform. *British Journal of Radiology*, *53*, 911–912.

LACZAY, A. and CSAPÓ, K., 1974. Luxatio ossis pisiformis? *Röntgen-Bild*, *27*, 463.

(*Author's reply*)

Isolated dislocation of the pisiform

THE EDITOR—SIR,

On behalf of my fellow authors and myself I would like to thank Dr. Laczay for the interest shown in our paper and his personal observations on the mobility of the pisiform. It would seem to me from this letter that Dr. Laczay questions our diagnosis because he feels loss of piso-triquetral parallelism may be seen under normal circumstances. He, however, ignores that in our discussion we referred to the pisiform being situated inferior and dorsal to its normal location and show in Fig. 1A that it was located between the ulna and triquetrum. In addition to showing loss of piso-triquetral parallelism on the lateral view, infero-dorsal displacement on the frontal view led to the diagnosis of a dislocated pisiform.

Dr. Laczay's own observations have shown the pisiform to show some mobility when the wrist is either flexed, extended or rotated. His observations, however, have not shown the pisiform to be located inferior and dorsal to its accustomed position when the wrist is in neutral position as was the case in Fig. 1A.

We therefore felt at the time and still do feel that this location of the pisiform conforms to Mather's description of a dislocated pisiform.

I would once again like to thank Dr. Laczay for his comments although his observations give us no cause to change our opinion on this case.

Yours, etc.,
M. SUNDARAM.

St. Louis University Medical Center,
St. Louis, Mo. 63104, USA.

(*Received January 1981*)

REFERENCE

MATHER, J. H., 1924. Dislocation of the pisiform bone. *British Journal of Radiology*, *29*, 17.

A new rectal marker for treatment planning

THE EDITOR—SIR,

The skin and subcutaneous tissues of the perineum are intolerant of irradiation and should therefore be excluded if possible from the treatment volume for tumours of pelvic

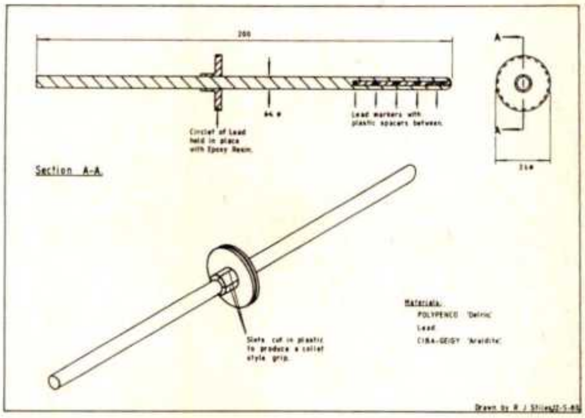

200
A
A
Circlet of Lead held in place with Epoxy Resin.
Lead markers with plastic spacers between.
Section A-A
Slots cut in plastic to produce a collet style grip.
Materials
POLYPENCO 'Delrin'
Lead
CIBA-GEIGY 'Araldite'
Drawn by R J Stiles

FIG. 1.

Construction of the marker.

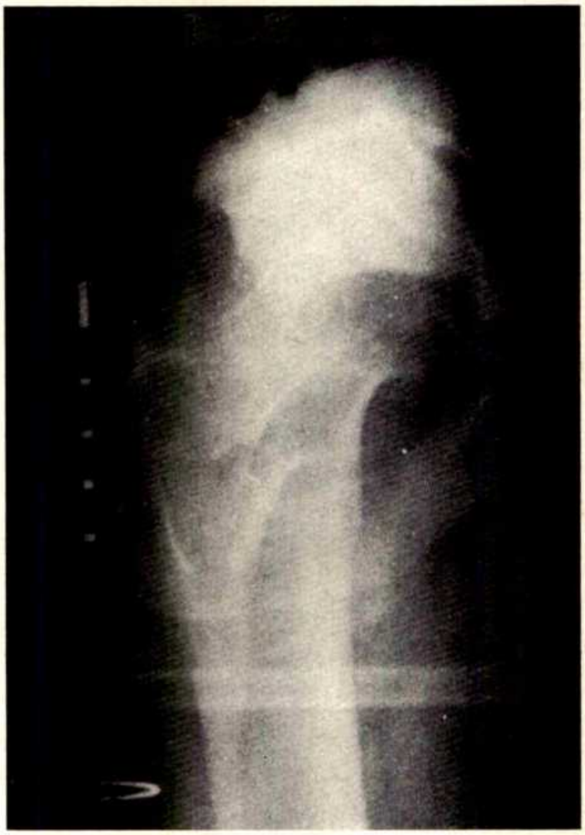


FIG. 2.

Marker in position in the rectum for planning a prostate treatment.

organs. Accurate localization of the skin surface is therefore essential. Further, the lower border of a tumour detected by digital examination may be localized on the planning film by relating it to the skin surface.

The perineal skin surface is not always clearly seen on the simulator screen or planning film. A modified rectal or vaginal marker has been devised to allow the skin level to be demonstrated and is shown in Fig. 1. It consists of a rod containing radio-opaque markers and a disc containing a radio-opaque ring. The disc slides along the rod, but grips it sufficiently to remain in the position set. Thus one may choose the length of rod which is to lie inside the patient. When used as a vaginal marker the rounded end is pushed into the posterior fornix. The patient then takes up the position for simulation of treatment with legs flat on the couch, and the disc is moved along the rod until it is firmly in contact with the skin whose position is thus localized. The rod is maintained in position by adhesive tape from its lower end to the abdominal wall or thigh. Figure 2 shows the device in use for planning a prostate treatment.

We should like to thank the Physics Workshop for making the device, and Mr. Roger Stiles for the drawing.

Yours, etc.,
M. A. Coe,
B. Baily.

Stanford Cade Department of Oncology
and Department of Physics,
Westminster Hospital,
London SW1.

(*Received June 1980 and in revised form October 1980*)

Media for single contrast knee arthrography

The Editor—Sir,

We recently carried out 60 single contrast knee arthrograms using non-ionic water-soluble contrast medium, in the radiology department of this hospital. Your readers may be interested in the results. The patients were selected on referral from an orthopaedic centre, and were aged between 18 and 49 years. There were 45 males and 15 females in the group. The contrast medium used was B1500 (300) known as Endomiro, containing 300 mg of iodine per ml, from Bracco of Italy. The films were subsequently compared with the next 60 referrals carried out using Conray 280. All patients were undergoing arthrography for the first time and 5 ml of contrast were used per examination.

Using Endomiro, no side-effects were noted. Slight extravasation occurred in three patients, which cleared up rapidly. In all cases the contrast medium was tolerated excellently. Visualization in those patients where no effusion was present (53) was excellent, and in the seven patients where there was a moderate to large effusion, visualization was adequate for diagnostic purposes.

No superior properties were found relative to Conray 280 for the purposes of single contrast arthrography. Endomiro was felt to be a very satisfactory contrast medium for this examination. Price, of course, may be a deciding factor, when B1500 is marketed.

Yours, etc.,
J. D. O'Connell.

Cork Regional Hospital,
Wilton, Cork, Ireland.

(*Received January 1981*)

Book review

Reflux Nephropathy. Edited by J. Hodson and Priscilla Kincaid-Smith. pp. viii+352, 1979 (Masson Publishing U.S.A. Inc., New York), $39.50.
ISBN 0-89352-044-6

We used to call it chronic pyelonephritis, a term that implied a clinical and radiographic syndrome that for mysterious reasons occurred in some children with vesico-ureteric reflux and infection. All is now revealed and explained—well, nearly all—in this book that will bring the reader rapidly up to date with this fascinating topic. It is the same old disease now more aptly, and by common consent, called *reflux nephropathy* which can be ignored by no-one who is seeing patients with urinary tract infections—paediatricians, urologists, nephrologists, radiologists, transplant surgeons and general practitioners.

This book is the Proceedings of a Workshop in 1978 and reads as easily as a "whodunit" and has many other similarities. The victim is the scarred kidney, the evil force is infected *intrarenal reflux*. It all seems so clear at first, but as the theme develops suspicion is thrown on other potential criminals. Could sterile reflux be harmful in a more diffuse way? Could the kidney have developed badly with predetermined areas of dysplasia as suggested by Douglas Stephens? Is the damage all caused by reflux back into the tubules, or may tearing of the fornices play a part? Is pressure a vital factor in whether or not intrarenal reflux occurs?

It is tempting to conclude that the *big bang theory* of scarring occurring with the first attack of urinary tract infection in the presence of intrarenal reflux is true, but other factors may well play a lesser role. Scars do matter. Nearly 20% of patients with reflux nephropathy become hypertensive, but at that stage it is still debatable as to whether surgery is helpful.

There is a clear need for standardization of radiological techniques and assessment of the findings such as the grading of reflux and the measurement of scars which may themselves take up to two years to mature. The need for some form of neonatal screening for intrarenal reflux is obvious, but the answer may be as much immunological as radiological. The surgical versus medical management argument continues with some 70% of spontaneous cessation of reflux and a 90%+ success rate for surgery, but the argument is not as simple as that.

This is mandatory and enjoyable reading. The chapters are clear and brief and the discussion between them poignant.

A final word of advice—read this book soon before the Proceedings of their next Workshop, as it may all be different and you will never know what you have missed.

R. H. Whitaker.

1981, *British Journal of Radiology*, 54, 367–372 APRIL 1981

Proceedings of The British Institute of Radiology

Radiobiology work-in-progress meeting: radiosensitizers and radioprotectors

Abstracts of papers presented at a British Institute of Radiology meeting held on Friday, November 21, 1980 in the Institute House, 32 Welbeck Street, London W1M 7PG (no reprints available)

Chairman: Professor R. J. Berry

Potentiation of radiation effect by the platinum drug, CHIP, by M. Laverick and A. H. W. Nias.
Further studies of the actions of radiosensitizers upon glutathione-deficient mutants of *Escherichia coli*, by H. A. Harrop, N. E. A. Crompton, W. Flitter, K. D. Held and B. D. Michael.
Radiosensitizing and cytotoxicity studies with CB 1954 (2, 4-dinitro-5-aziridinyl-benzamide), by I. J. Stratford, C. Williamson, S. Hoe and G. E. Adams.
Hypoxic-cell radiosensitization *in vivo*: studies with a homologous series of 2-nitroimidazoles, by D. J. Chaplin, P. W. Sheldon, I. Ahmed, I. J. Stratford and G. E. Adams.
Mechanisms of *in vitro* cytotoxicity of radioprotective WR-2721, by J. M. Gaugas.
Radioprotection by WR-2721 in normal mouse skin and tumour, by A. M. Rojas and F. A. Stewart.
The radioprotecting drug WR-2721—time course studies, by E. L. Travis, A. M. de Luca, T. N. Padikal and J. F. Fowler.
Modification of tumour and host response to chemotherapy by misonidazole or by WR-2721, by P. R. Twentyman.
Pharmacokinetic aspects of interactions between nitroimidazoles and other drugs, by P. Workman.
The neurotoxicity of hypoxic-cell radiosensitizers, by Claire Clarke, K. B. Dawson and P. W. Sheldon.
Does misonidazole sensitize normal brain to radiation? by S. B. Field and C. C. Morris.

POTENTIATION OF RADIATION EFFECT BY THE PLATINUM DRUG CHIP

By M. Laverick and A. H. W. Nias

Richard Dimbleby Department of Cancer Research,
St. Thomas's Hospital Medical School, London SE1

This investigation involves the use of a potential chemotherapeutic agent as a sensitizer of hypoxic cells to X-irradiation. It is well established that certain platinum complexes of the *cis* configuration are potent antitumour agents in their own right. We now report the effect of the platinum complex *cis*-dichloro-*bis* (isopropylamine) trans-dihydroxy-platinum-IV (CHIP) given as a pretreatment to *in vitro* cultures of Chinese hamster ovary (CHO) cells and C_3H mouse mammary tumour cells.

CHIP was given as a one hour pretreatment at 37°C with varying time intervals before X-irradiations under aerated and hypoxic conditions. Time intervals of one, three, five, and 24 h between drug and radiation in hypoxic CHO cells gave dose modifying factors (DMF) of 1.7, 1.9, 1.36 and 1.0 respectively. The extrapolation numbers N remained unaltered. A one hour delay in drug and radiation treatment of aerated CHO cells gave a much lower DMF of 1.1 but the extrapolation number was reduced.

C_3H mouse mammary tumour cells showed no potentiation of aerated cells by CHIP to damage by X rays. Potentiation was only observed under hypoxia. A maximum DMF of 1.7 was obtained after a one to three hours delay between drug and radiation treatment. By five hours the DMF was reduced to 1.14 and at eight hours no enhancement of cell killing was observed.

Under optimal conditions of drug and X-irradiation (one hour delay), the effect of pretreatment by CHIP on hypoxic cells is manifested not only as a decrease in D_0 which is measured by DMF, but also as a reduction in the "shoulder region" to a point where survival is identical to that observed in aerated X-irradiated tumour cells. These results emphasize the importance of finding the optimal regimes of drug dose and timing of the subsequent X irradiation.

The work was supported by a Cancer Research Campaign Grant.

FURTHER STUDIES OF THE ACTIONS OF RADIOSENSITIZERS UPON GLUTATHIONE-DEFICIENT MUTANTS OF *ESCHERICHIA COLI*

By H. A. Harrop, *N. E. A. Crompton, †W. Flitter, K. D. Held and B. D. Michael

Cancer Research Campaign Gray Laboratory,
Mount Vernon Hospital, Northwood, Middlesex HA6 2RN
**Strahlenzentrum, Justus-Liebig-Universität, Giessen,*
W. Germany
and
†School of Biological Sciences,
Brunel University, Uxbridge, Middx. UB8 3PH

We have compared the actions of oxygen and other radiosensitizers in a range of related *E.coli* K12 strains which have various deficiencies in their glutathione (GSH) synthetic pathways (Apontoweil and Berends, 1975). The strains are: AB1157, which is a wild type proficient in GSH synthesis; strain 830, which is deficient in GSH synthetase, the final enzyme of the GSH synthesis pathway; and strains 7 and 821, which are both deficient in γ-glutamyl cysteine synthetase, the enzyme required for the penultimate step of GSH synthesis.

Strains 1157 and 830 showed similar oxygen enhancement ratios (OER) of 3.9; but for strains 7 and 821 the OER was found to be considerably lower at 2.8. The oxygen K-values (concentration of O_2 to give half the maximal effect) were found to be 0.7% for strain 1157, 0.26% for strain 830 and 0.06% for strains 7 and 821. Thus with enzyme deficiency at the earlier stages of the GSH pathway, the OER was reduced and the K-curves were displaced to lower concentrations by about a factor of 0.1.

We have determined the curves of concentration vs. enhancement ratio in these strains for the radiosensitizers misonidazole, metronidazole, 5-chloro-1-methyl-4-nitroimidazole (CMNI) and triacetoneamine-N-oxyl (TAN). Comparing the concentrations required to achieve an enhancement ratio of 2.0 in these strains, misonidazole showed an overall displacement factor of about 0.1 as found with oxygen. In contrast, none of the other compounds tested showed this displacement, with the possible exception of TAN, where a relatively slight shift was evident. Thus it appears that when genetic differences of GSH synthesis are used to manipulate intracellular SH levels, the responses to various sensitizers are different.

REFERENCE

APONTOWEIL, P. and BERENDS, W., 1975. Isolation and initial characterization of glutathione-deficient mutants of *E.coli* K12. *Biochemica et Biophysica Acta, 399*, 10–22.

RADIOSENSITIZING AND CYTOTOXICITY STUDIES WITH CB 1954 (2, 4-DINITRO-5-AZIRIDINYLBENZAMIDE)

By I. J. Stratford, C. Williamson, S. Hoe and G. E. Adams

Physics Department, Institute of Cancer Research,
Sutton, Surrey, SM2 5PX

The nitroaromatic compound CB 1954 is a monofunctional alkylating agent and has previously been shown to be a potent and selective inhibitor of the Walker 256 tumour. This compound possesses molecular and structural features which have suggested that it may be active as a radiosensitizer of hypoxic mammalian cells. Previously, we have shown that electron affinity, as measured by the one-electron reduction potential E^1_7, is the major factor influencing sensitizing efficiency *in vitro*. For CB 1954 the $E^1_7 = -385$ mV, which is similar to misonidazole. However, the ability of this compound to sensitize hypoxic cells is considerably greater than that of misonidazole, *e.g.* 0.2 mM CB 1954 gives an enhancement ratio of 2.2 compared to 1.45 for the same concentration of misonidazole.

2-Phenyl-4(5)-amino-5(4)-carboxamide (phenyl-AIC) can protect against the cytotoxic action of CB 1954. Further, when cells were irradiated in the presence of CB 1954 and phenyl-AIC, sensitization was reduced to a level similar to that seen for misonidazole, indicating that phenyl-AIC can protect against part of the sensitization caused by CB 1954. The additional sensitization seen with CB 1954 may be associated with the alkylating activity of this compound; if this is true it may have considerable implications for the development of new radiosensitizing drugs.

HYPOXIC-CELL RADIOSENSITIZATION *IN VIVO*: STUDIES WITH A HOMOLOGOUS SERIES OF 2-NITROIMIDAZOLES

By D. J. Chaplin, P. W. Sheldon, I. Ahmed, I. J. Stratford and G. E. Adams

Physics Department, Institute of Cancer Research,
Sutton, Surrey SM2 5PX

The neurotoxic side-effects which have been experienced clinically with the hypoxic-cell radiosensitizer misonidazole have necessitated the development of a less toxic and preferably more efficient agent. As part of this development, the effect of increasing the side-chain length (*n*) on the radiosensitizing efficiency and toxicity *in vivo* is being evaluated using a homologous series of 2-nitroimidazole compounds.

Acute toxicity studies ($LD_{50/2d}$) have shown that for both intraperitoneal and intravenous administration toxicity increases with increasing chain length; this corresponds to the increasing octanol: water partition coefficients of these compounds. However, after oral administration, compounds of $n=4$, 5 and 6 are less toxic than those of shorter ($n=2$) or longer ($n=8$ or 11) chain length.

At equitoxic doses (¼ of the $LD_{50/2d}$), sensitizer enhancement ratios of 1.6, 1.5, 1.3, 1.1, 1.2, and 1.2 were obtained for $n=2$, 4, 5, 6, 8, and 11 respectively. However, on administration of the maximum tolerated doses, $n=4$ was optimal for the Lewis lung tumour giving an SER of 1.75.

MECHANISMS OF *IN VIVO* CYTOTOXICITY OF RADIOPROTECTIVE WR-2721

By J. M. Gaugas

Cancer Research Campaign Gray Laboratory,
Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

WR 2721 [$NH_2(CH_2)_3NH(CH_2)_2SH_2PO_3$] is known to protect normal rather than neoplastic tissue against radiation damage *in vivo*. When WR-2721 was added to cultured cells (Bri8) there was arrest of proliferation due to diverse mechanisms (Gaugas, 1981). WR 2721 was oxidized to the "thiolaminoaldehyde" antiproliferogen by polyamine oxidase (PAO) in fetal-calf serum (FCS, 10% supplement in medium). Optimally, the 50% inhibitory dose (ID_{50}) for cell arrest was 150 μM WR 2721 at 7.5 μg/cm³ of purified PAO, *i.e.* equivalent to use of 24% FCS in cultures. Prior addition of excess catalase to cultures with WR 2721 failed to reduce cytotoxicity, and thereby eliminated H_2O_2 byproduct as the antiproliferogen in the system. Addition of reduced, but not oxidized, biogenic glutathione, L-cysteine and DL-homocysteine (> 1.0 mM) partially prevented cytotoxicity due to thiolaminoaldehyde adduction with SH compounds.

Inactivation of PAO with Na semicarbazide (50 μM), aminoguanidine (150 μM) or 3-hydroxybenzyloxyamine (1.0–10 μM), which themselves were not cytotoxic, completely prevented WR 2721 oxidation and raised the ID_{50} to 4.5 mM (above a level of clinical relevance). Since PAO occurs in liver, this WR 2721 conversion and SH adduction should be of pharmacological interest. Combined administration of a PAO inhibitor drug (pyridoxal and/or flavin co-factor inactivation) together with WR 2721 might spare its radioprotective capability or decrease cytotoxicity to benefit tumour radiotherapy.

REFERENCE

GAUGAS, J. M., 1981. Mechanisms of *in vitro* cytotoxicity of S-2-(3-aminopropylamino) ethylphosphorothioic acid. In "*Polyamines in Normal and Neoplastic Cells*", Ed. V. Zappia and C. M. Caldarera. (Advances in Polyamine Research, Vol. 3) (Raven Press, New York) (In press).

RADIOPROTECTION BY WR 2721 IN NORMAL MOUSE SKIN AND TUMOUR

By A. M. Rojas and F. A. Stewart

Cancer Research Campaign Gray Laboratory,
Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

Radiation protection of normal mouse skin and a mouse fibrosarcoma by the thiol compound WR 2721 has been measured for a range of drug doses using single treatments of X rays and the protector. The WR 2721 was administered i.p. 30 minutes before irradiation. Tumours (implanted subcutaneously on the ventral thorax) were irradiated under sodium pentobarbital anaesthesia, and skin (of the left hind foot) was irradiated on unanaesthetized mice in oxygen.

The protective action of WR 2721 was assessed by comparing X-ray dose response curves with and without drug. In both skin and tumour there was no significant X-ray protection using a drug dose of 200 mg/kg. Using 400–600 mg/kg WR 2721 the maximum protection factor observed for skin was 1.5 and for the tumour was 1.2 to 2.0. The extent of radioprotection was found to vary with X-ray dose for both skin and tumour. The protection observed in the skin was *not* greater than that observed in the tumour and no therapeutic advantage was gained.

Combinations of the hypoxic-cell radiosensitizer misonidazole (200 mg/kg) and the radioprotector WR 2721 (500 mg/kg) were also tested. Skin radioprotection was reduced from 1.5 to 1.2 in the presence of misonidazole; tumour radiosensitization was reduced from SER 1.7 (misonidazole alone) to 1.1 in the presence of WR 2721. The data suggest a direct competition between these radiosensitizing and radioprotective drugs. The combined use of misonidazole and WR 2721 for this particular tumour was not found to give a therapeutic advantage over X rays alone.

THE RADIOPROTECTING DRUG WR 2721—TIME COURSE STUDIES

By E. L. Travis, A. M. de Luca, T. N. Padikal and *J. F. Fowler

Radiation Oncology Branch, NCI, Building 10, Room B3B/38 NIH Bethesda, MD 20205, USA

WR 2721 is a phosphorothioate which has been reported to protect animals against radiation marrow death ($LD_{50}/30$ days) by a dose modifying factor (DMF) of about 2.7, and mice against acute skin reactions by a DMF of 1.6–2. Its therapeutic interest is because it has been reported to penetrate poorly into 16 out of 17 types of mouse and rat tumour tested.

In the present experiments the radioprotective effect of 400 mg/kg WR 2721 has been investigated over a series of times from five to 60 min after intravenous or intraperitoneal injection. The acute desquamation in one hind limb of mice was studied. DMFs of 1.6–2.1 were obtained at 30 to 60 min, in agreement with previously published work, but only 1.1–1.3 at five minutes, and intermediate values at ten and 15 minutes.

---

*On sabbatical from Gray Laboratory, Mount Vernon Hospital, Northwood, Middx. HA6 2RN.

MODIFICATION OF TUMOUR AND HOST RESPONSE TO CHEMOTHERAPY BY MISONIDAZOLE OR BY WR 2721

By P. R. Twentyman

MRC Clinical Oncology and Radiotherapeutics Unit, Hills Road, Cambridge CB2 2QH

The effect has been studied of adding either misonidazole (MISO) or the radioprotective drug, WR 2721, to conventional cytotoxic drug therapy of the KHT and RIF-1 sarcomas in C3H mice. At a dose of 1 mg/g, MISO increased the growth delay produced by low doses of cyclophosphamide (CTX), but at doses greater than about 60 mg/kg of CTX, the response curves were parallel. At a lower dose of MISO (0.33 mg/g) the effect was largely lost and little modification of CTX response was seen. The response of the KHT tumour to BCNU was only marginally increased by the simultaneous administration of 1 mg/g of MISO. In combination with CCNU, 0.5 mg/g of MISO produced a considerably increased growth delay in both tumours, in agreement with the recent finding of Siemann (1981). Once again, however, the principal effect appeared to be reduction of shoulder rather than dose-modification.

The tumour growth delay produced by CTX was reduced if WR 2721 (400 mg/kg) was given 30 min earlier. At a CTX dose of 75–100 mg/kg the dose modifying factor (DMF) was 0.7–0.8, but in the RIF-1 tumour it was not so low at higher doses of CTX.

Determination of the LD_{50} for CTX showed a DMF of 1.2–1.3 for MISO (0.33 mg/g) and about 0.8 for WR 2721 (400 mg/kg). Neither modifying agent appeared to cause any consistent change in the pattern of body weight loss following CTX, but WR 2721 reduced the myelosuppression seen at three to four days after CTX.

These results suggest that little change in CTX response is likely to be produced by the addition of clinically relevant doses of MISO. The protective effect of WR 2721 (400 mg/kg) in combination with CTX is not confined to normal tissues and may be as great in terms of tumour response as in terms of acute LD_{50} in this system.

REFERENCE

Siemann, D. W., 1981. The *in vivo* combination of the nitroimidazole misonidazole and the chemotherapeutic agent CCNU. *British Journal of Cancer*, (in press).

PHARMACOKINETIC ASPECTS OF INTERACTIONS BETWEEN NITROIMIDAZOLES AND OTHER DRUGS

By P. Workman

MRC Clinical Oncology and Radiotherapeutics Unit, Hills Road, Cambridge CB2 2QH

We have been interested in the pharmacokinetics of interactions between nitroimidazoles and other drugs, (1) as experimental probes and (2) as possible means of reducing neurotoxicity. The hepatic microsomal enzyme-inducers phenobarbitone and phenytoin increased the clearance of misonidazole and lipophilic analogues through more rapid metabolism, but did not affect the pharmacokinetics of hydrophilic analogues such as desmethylmisonidazole. When evaluated as potentially superior enzyme inducers, antipyrine was less effective than phenobarbitone in mice whereas pregnenolone-16α-carbonitrile (SC-4674, Searle) was about equally effective. Dexamethasone had no effect on misonidazole metabolism in mice but in some circumstances reduced misonidazole brain levels.

Dexamethasone or inducers of oxidative metabolism such as phenobarbitone and phenytoin may reduce misonidazole neurotoxicity. Alternatively, if nitroreduction is involved in the toxic mechanism, inhibition of this pathway might be effective. The enzyme xanthine oxidase can act as a nitroreductase and is inhibited by allopurinol. Interaction between allopurinol and misonidazole in mice was reported recently by Raleigh *et al.* (1980). We have shown that allopurinol pretreatment (32 mg/kg/day i.p. for five days) did not change the pharmacokinetics of misonidazole or desmethylmisonidazole in mice. Given as a single dose (32 mg/kg i.p.) 30–60 min before, allopurinol had little or no effect on the clearance of misonidazole or the more lipophilic analogue Ro 07–0913. In contrast, the clearance of the more hydrophilic desmethylmisonidazole (as a metabolite or injected drug) and SR–2508 was considerably reduced. These data suggest that the presence of allopurinol may reduce the renal clearance of hydrophilic nitroimidazoles.

REFERENCE

Raleigh, J. A., Shum, F. Y., Koziol, D. R. and Saunders, W. M., 1980. Structure-function dependence and allopurinol inhibition of radiosensitizer/nitroreductase interaction. *Cancer Clinical Trials, 3*, 55–62.

THE NEUROTOXICITY OF HYPOXIC-CELL RADIOSENSITIZERS

By Claire Clarke, K. B. Dawson and P. W. Sheldon

Radiobiology Unit, Department of Physics, Institute of Cancer Research, Sutton, Surrey SM2 5PX

A quantitative, cytochemical method has been developed to measure lysosomal enzyme activity in the peripheral nerves of mice following treatment of animals with hypoxic-cell radiosensitizers. The β-glucuronidase and acid phosphatase activities increased to a maximum at three to four weeks after misonidazole treatment. These changes were greater in the distal than in the proximal regions of the nerves, which is indicative of a dying-back neuropathy. Increased lysosomal activities were related to the drug dose administered and were significantly elevated at clinically relevent levels of misonidazole. Furthermore, these changes could be correlated with behavioural studies using a simple functional test.

These time related increases were not peculiar to misonidazole but were also observed following administration of a 4- and 5-nitroimidazole.

Other hypoxic-cell radiosensitizers have been studied to evaluate the possible role of lipophilicity in neurotoxicity. A homologous series of compounds of increasing lipophilicity showed increased neurotoxicity with increased chain length, although the interpretations of these differences are complex and depend upon the drug absorption, distribution and elimination.

DOES MISONIDAZOLE SENSITIZE NORMAL BRAIN TO RADIATION?

By S. B. Field and C. C. Morris

MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

A frequent complication in the clinical use of misonidazole is the occurrence of peripheral neuropathies. It has also been observed in various normal tissues that the drug enhances the effect of ionizing radiation, presumably due to a small component of hypoxic cells in these tissues. It is therefore important also to question whether the drug enhances radiation damage to the CNS.

Our experiments were aimed at measuring whether the drug enhanced radiation damage in the rodent brain. The method used was to count cells in the subependymal layer of the rat forebrain. These cells divide throughout life, adding to the glial cell population. They are present in man although their mitotic activity decreases with age.

Eight-week old rats were used. They were anaesthetized for irradiation. The decrease in the number of cells was measured at 30 days after irradiation for a range of doses of X rays. This was done for radiation alone and with misonidazole given at 1 mg/g body weight at 45 min before irradiation. The misonidazole alone caused no reduction in the number of cells and made no difference in the response to radiation. Since it is known that the drug does cross the blood brain barrier the result implies that these cells in the brain are fully oxygenated.

Whole body irradiation

Abstracts of papers presented at a meeting held on Thursday, November 20, 1980 at the British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (no reprints available)

Chairman: Dr. M. J. Day

Distribution of dose in whole-body irradiation, by G. P. Lawrence.
Total-body irradiation, by A. Barrett.
Whole-body irradiation in Non-Hodgkin's lymphoma, by J. A. Bullimore.
Total-body irradiation in advanced Non-Hodgkin's lymphoma, by H. J. Dobbs.
Half-body irradiation for treatment of metastatic prostatic carcinoma and plasma cell myeloma, by C. G. Rowland.

DISTRIBUTION OF DOSE IN WHOLE-BODY IRRADIATION

By G. P. Lawrence

Physics Department, Royal Marsden Hospital, Sutton, Surrey

In most centres where whole-body irradiation is undertaken, therapy units of conventional design are used. The limited facilities available have therefore dictated the techniques developed.

The technique described here evolved over a number of years at the Royal Marsden Hospital. A cobalt-60 unit is used, with the beam pointing horizontally to obtain a large enough radiation field. The patient is treated in a Perspex cot and lies in three positions: on the right and left sides and supine. In each position the patient is irradiated with equally weighted opposing fields.

A calibration irradiation is done about one week before the treatment, when the sum of the entrance and exit doses on the skin is determined at different levels of the patient in each of the three positions. From the doses measured the treatment is prescribed in terms of the time spent in each position.

A variation in dose is observed not only along the length of the patient but also in transverse planes.

With a field size larger than the patient, the source-skin distance and the size of the patient determine the depth dose. As both factors increase so the dose at a given depth increases. The patient's shape at each level results in considerable variation of dose in each plane, but this effect is reduced by treating the patient in a number of positions.

The variation observed along the length of the patient is due to varying thickness, the patient's position and the shape of the beam. The effects are reduced by carefully selecting the proportion of time spent in each position, by judicious positioning of the patient and by the use of tissue-equivalent bolus to reduce the variation in the patient's width.

TOTAL-BODY IRRADIATION

By A. Barrett

Radiotherapy Unit, Royal Marsden Hospital and Institute of Cancer Research, Sutton, Surrey SM2 5PT

From the early part of this century total-body irradiation (TBI) has been used as a treatment for radiosensitive tumours but doses were limited to less than 300 cGy (rad) because of bone-marrow toxicity. With the discovery of the HLA system and better understanding of immunological mechanisms, bone-marrow transplantation became feasible in the 1960's, and was introduced in Seattle as a treatment for acute leukaemia which had failed to respond to conventional treatment. Patients were prepared for transplantation with cyclophosphamide and 1000 cGy (rad) TBI which prevented graft rejection and killed residual leukaemic cells. Radiation seems to be a most important element in this preparation and intensive drug regimes alone are less effective. With patients in relapse, early death after transplantation (related to general condition, amount of previous chemotherapy, etc.) was a major problem and this has led to a policy of grafting in remission.

Doses of 1000 cGy (rad) to the whole body have been given in various centres using different machines, dose rates and methods of estimating dose received. It has therefore been possible to determine the tolerance of specific organs to single high doses of radiation.

Critical organs seem to be the lungs and the liver. Interstitial pneumonitis remains a major problem with a high mortality rate in most centres. This complication is related to total dose and may be avoided by low dose-rate treatment or fractionation and by control of graft-versus-host disease (GVHD). Veno-occlusive disease of the liver seen after grafting may be related to irradiation. Transient pancreatitis and parotiditis are seen but do not lead to permanent damage. Cataracts develop in 50% of patients by three to five years. Amenorrhoea and sterility may be expected although they may not be absolute. Other hormonal functions are unaffected.

Studies at present under way are designed to increase control of leukaemia by increasing the radiation dose without producing more damage to normal tissues. Several American centres are giving doses between 1200 and 1750 cGy (rad) in three to seven days to try to achieve this. The same effect may be obtained by irradiation with a single fraction at very low dose rates.

WHOLE BODY IRRADIATION IN NON-HODGKIN'S LYMPHOMA

By J. A. Bullimore

Radiotherapy Centre, Bristol Royal Infirmary

Twenty-six patients with non-Hodgkin's lymphoma, unresponsive to or in relapse following chemotherapy, received total-body irradiation (TBI) to a dose of 150 cGy (rad) in 15 fractions over 18 days. A response was achieved with 17 patients, in six of whom it was complete. The actuarial survival rates were 50% at one year and 42% at 30 months. Best results were achieved in those with low-grade histology and in those under 60 years of age. Transient marrow toxicity was the only significant side-effect of treatment; although it was usually severe, there were no serious sequelae. TBI should be considered as a secondary therapy in non-Hodgkin's lymphoma, regardless of previous treatment.

TOTAL-BODY IRRADIATION IN ADVANCED NON-HODGKIN'S LYMPHOMA

By H. J. Dobbs

Department of Radiotherapy, The Royal Marsden Hospital, Sutton, Surrey SM2 5PT

Total body irradiation (TBI) has been shown in a randomized trial to give similar response and survival rates to combination chemotherapy in the treatment of lymphomas (Johnson *et al.*, 1978). Between 1973 and 1977, 37 patients with Stage III and IV non-Hodgkin's lymphoma were treated at the Royal Marsden Hospital. Twenty-four patients had received no previous therapy. Patients with nodular lymphoma were treated on evidence of progressive disease.

TBI of 1.5 Gy (150 rad) MPD was given in ten fractions and 12 days or ten fractions treating twice weekly. Eleven patients received hemibody irradiation of 3 Gy (300 rad) MPD in ten fractions and 12 days.

The complete response rate in 22 patients with nodular lymphoma was 64% compared to 40% in the 15 patients with diffuse disease. The overall response rate was 73% for the nodular and 80% for the diffuse lymphomas.

The median duration of response was 12 months (range 2 to 41). There was no difference between the median duration in those whose response was complete and in those with partial response, nor in those who had received no previous treatment compared with those who had.

Bone marrow toxicity was the major complication but there was no incidence of serious haemorrhage. Fourteen out of 37 (38%) of patients had platelet counts $< 50000/\text{mm}^3$ and in six of these no further chemotherapy was possible. All six had involvement of the bone marrow and five of them had received hemibody irradiation. Two patients developed clinical hypothyroidism.

The overall response rate of 76% is similar to that achieved with chemotherapy and is without serious toxicity. Subsequent chemotherapy was given successfully except in those patients with prolonged thrombocytopenia which appeared to be related to an involved bone marrow.

Survival is not improved by TBI at these doses but higher doses may become feasible with advances in transplantation.

The patients reported are under the care of Professor M. J. Peckham and Dr. T. J. McElwain.

REFERENCE

Johnson, R. E., Canellos, G. P., Young, R. C., Chabner, B. A. and DeVita, V. T. 1978. Chemotherapy (cyclophosphamide, vincristine, and prednisone) versus radiotherapy (total body irradiation) for Stage III–IV poorly differentiated lymphocytic lymphoma. *Cancer Treatment Reports, 62*, 321–325.

HALF BODY IRRADIATION FOR TREATMENT OF METASTATIC PROSTATIC CARCINOMA AND PLASMA CELL MYELOMA

By C. G. Rowland

Radiotherapy Centre, Bristol Royal Infirmary

High-dose radiation therapy as a single fraction to the upper and lower halves of the body provides effective palliation of widespread malignant disease, particularly in tumours believed to have a slow doubling time such as prostate, gut and myeloma. Some 100 patients are treated each year by this method in Bristol at the present time.

The radiation is delivered by an 8 MeV linear accelerator at 200 cm SSD, with a tissue maximum of 750 cGy (rad) given to the upper half of the body and 1000 cGy to the lower half, the two treatments being spaced one month apart to allow bone-marrow recovery in the untreated half. A pre-treatment infusion of 500 ml normal saline containing 20 ml potassium and 100 mg hydro-cortisone is given before each treatment. This appears to be effective in limiting the immediate effects of radiation sickness. Another short-term side effect is swelling of the salivary gland, which resolves spontaneously within one to two days. Long-term complications include epilation and xerostomia which revert to normal after about six months.

Thirty patients with metastatic prostatic carcinoma have been treated after previous treatment with hormones, chemotherapy or localized irradiation. Bone-marrow examination in the first 15 patients showed gross involvement in all cases. Twenty-one patients were dead within 12 months. Significant immediate relief of pain was produced in 22/30 patients (73%). This was maintained until death in 20/30 patients (67%). It is of interest that three patients are alive and free of pain at 36, 24 and 24 months.

In a separate study, five patients with plasma-cell myeloma and high tumour-cell mass have been treated by HBR. Three patients are alive at 25, 24 and 24 months. The percentage of plasma cells in the upper and lower half of the body and the plasma immunoglobulins have been significantly reduced at six months. This study clearly shows that single doses of radiation reduce the number of tumour cells by a factor of about 100 in humans. It seems possible that in some tumours a medium survival equivalent to that obtained by present day chemotherapy can be achieved by half-body irradiation with minimal toxicity, indeed perhaps in myeloma radiation should be considered before chemotherapy.

Book reviews

Perceptions of Risk (*Proceedings of the Fifteenth Annual Meeting of the National Council on Radiation Protection and Measurements*). pp. 191, 1980 (NCRP, Washington, DC), $15.00.
ISSN 0195–7740

The symposium on "Perceived risk", which took place during the NCRP meetings in March 1979 in Washington, reviewed this elusive subject courageously and well. A great deal has been written in recent years on the numerical evaluation of the size of various types of risk. Much is also being written about the way in which people compare the importance of different kinds of risk. The papers given at this symposium and their discussions, which are reported in full in this volume of proceedings, give useful, thoughtful and often very revealing surveys of a number of factors which affect this "perceptior" of risk. Margaret Maxey discusses the problems involved, particularly in legislation, when no threshold for harmful effects can be supposed to occur; Roy Albert has a good review of the problems of dealing with the possible carcinogenicity of chemicals; and Victor Bond looks at the vexed question of an "acceptable" risk. Quantitation appears in Paul Slovic's reports of the way in which different groups of people thought different types of risk differed in magnitude or should be assessed, and the social impact that they attach to death from different, chiefly environmental, causes. Actuarial procedures on risk are discussed by James Hickman, and the concern of organized labour with a reduction of risk to the lowest technically feasible levels, rather than by any cost benefit optimization, by George Taylor. Ida Hoos describes societal anxieties about supposedly inadequate data on radiation levels and effects in different circumstances. The panel discussion also includes a stimulating review of the value of the legal process in assessing social detriments and the idea of a "Science Court".

The proceedings also include the text of Hymer Fridell's Lauriston Taylor lecture on "Radiation Protection—Concepts and Trade offs", a paper by Taylor himself on the past 50 years of radiation protection, and a valuable review by Charles Land on the role of neutrons in causing late effects amongst A-Bomb survivors.

Edward Pochin.

Mathematics for technologists in radiology, nuclear medicine, and radiation therapy. By S. S. Stefani, L. B. Hubbard and E. Sanders. pp. viii + 240, illus. 1979 (YB Medical Publishers, London; C. V. Mosby, Chicago), £2·25.
ISBN 0–8016–4762–2

This small volume, produced in soft covers, was stimulated by a survey held by one of the authors which showed that American high school graduates were not sufficiently prepared in mathematics for successful careers in radiologic technology. It presents clearly and concisely the fundamentals of mathematics in eleven chapters which progress from simple arithmetic, algebra and geometry through to accounts of exponential formulation, statistics and elementary calculus. The presentation reflects the usual American custom by including questions at the end of each chapter but answers are provided only to selected problems and the basis of this selection is not always clear. Illustrative examples, formulae and figures have all been numbered serially but the numbers do not correspond with each other, leading to some confusion for the reader.

The overall approach is unlikely to be the same as that currently taught in schools in the United Kingdom but nevertheless this volume will provide a useful source for rapid revision. It can be recommended for inclusion in the libraries of schools of radiographers and some students will doubtless wish to have their own copies.

J. Roylance.

Forthcoming events

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

BIR Annual Congress 1981 and Scientific Exhibition

The British Institute of Radiology Annual Congress will be held on April 9–10, 1981 at the Royal Free Hospital and will include the Mackenzie Davidson Memorial Lecture by R. G. Grainger on "Intravascular contrast media—present perspectives". Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

Echocardiography

A course in Echocardiography will be held at Harefield Hospital from April 27 to May 1, 1981. The course is intended for those having experience in cardiac ultrasound and working in the field. Accommodation available. Further details from Mrs. M. Beech, telephone Harefield 3737, ext. 609.

BIR Meetings, May 1981

Thursday, May 14: State of the Art Seminar on Preparation of the Bowel Prior to Radiology (Chairman, Dr. G. J. de Lacey) at 17.45; and Radiology of the Colon (speakers: C. Bartram, C. Wastell, C. Williams) at 19.40. Friday, May 22: Radiobiology work-in-progress meeting on Hyperthermia, at 11.00. Titles and abstracts to Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, by April 7.

Annual General Meeting

The Annual General Meeting of the Institute will be held on Thursday, May 14, 1981. All members will receive notification.

Fourth European Congress on Ultrasonics in Medicine

This will be held in Dubrovnik, May 17–24, 1981, sponsored by EFSUMB and organized by the Yugoslav Association of Societies for Ultrasound in Medicine and Biology. Information from Dr. Višnja Latin, M.D., D.Sc., President of the Organizing Committee, Jagode Truhelke, 26, 41090 Zagreb, Yugoslavia.

The Marie Curie Memorial Foundation, London
Thirteenth Annual Symposium
Cancer—A Panoramic View

Thursday, May 28, in the Edward Lumley Hall, the Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2A 3PN. Chairmen: Mr. R. W. Raven and Dr. F. J. C. Roe. Other speakers: Prof. D. V. Parke, Prof. R. W. Baldwin, Mr. R. Tiffany, Prof. A. Lant, Dr. N. Finter, Prof. K. Hellmann, Dr. I. W. F. Hanham and Mr. I. Burn. Fee £10·50. Applications and information: Mr. G. D. Steward, Assistant Secretary, The Marie Curie Memorial Foundation, 124 Sloane Street, London SW1X 9BP (phone 01–730 9157).

Fifth Congress of the European Nuclear Medicine Society
Nineteenth Congress of the Societa Italiana di Biologia e Medicina Nucleare

Pisa, June 9–12, 1981. Main suggested topics: cardiovascular applications of radionuclides *in vivo* and *in vitro*; advances in regional lung morphofunctional studies; development of radioimmunoassay in comparison with non-radioactive immunochemical techniques; advances in nuclear imaging in comparison with alternative techniques. Official language: English. There will also be an industrial and technical exhibition.

Registration forms and other information from: The Organizing Secretariat, OIC, Via G. Modena 19, 50121 Florence, Italy. (Registration by April 15, 1981).

Study Day
The Role of the Plain Abdominal X-ray in the Acute Abdomen

Wednesday, June 24, 1981, Kent Postgraduate Medical Centre at Canterbury. A comprehensive and critical analysis of the plain abdominal radiograph and its correlation with operative and post-mortem findings.

Aimed at SHO's, registrars and senior registrars in surgery and radiology, particularly those preparing for Fellowship examinations. (The event has been approved for Study Leave.)

Fee £20 including coffee, lunch and tea. Details from Postgraduate Administrator, Kent Postgraduate Medical Centre, Kent and Canterbury Hospital, Canterbury CT1 3NG.

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Programme from: ICR81, c/o Brussels International Trade Fair, Parc des Expositions B-1020, Brussels, Belgium.

First International Symposium on Minimal Invasive Cancer

Organized by the University Clinic of Obstetrics and Gynaecology, Graz, Austria, to be held at the Kongresshaus, Graz, July 1–4, 1981. Language: English. Main topics: cervix, vulva, endometrium, breast, oesophagus, stomach, large intestine, lung, thyroid, urinary bladder, prostate, larynx, oral cavity, skin, other organs. Enquiries: Interconvention, PO Box 105, A-1014, Vienna, Austria (phone (0222) 57 62 88). President: Prof. E. Burghardt; Secretary General, Dr. E. Holzer.

Uroradiology Cambridge 1981
Trinity Hall, July 9–10

This is the third Cambridge summer meeting, designed for consultants and senior registrars. About half the time is given to open discussion. Speakers will include Dr. R. G. Grainger, Dr. I. Kelsey Fry, Mr. R. H. Whitaker, Dr. H. M. Saxton, Professor S. R. Meadow, Mr. P. G. Ransley, Dr. A. J. Davidson (San Francisco) and Dr. L. B. Talner (San Diego).

The meeting is limited to 65 residential members. Cost £55—full details from Professor T. Sherwood, Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ (phone Cambridge (0223) 45171).

Forthcoming events

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

23rd Annual Meeting
American Association of Physicists in Medicine
9–13 August, 1981

The 23rd Annual Meeting of the American Association of Physicists in Medicine (AAPM) will be held at the Sheraton Boston Hotel, Boston, MA on August 9–13, 1981. Submitted papers and exhibits in basic, clinical, technical, or applied medical physics are solicited for this meeting. Both members and non-members of the AAPM are cordially invited to participate. For additional information contact J. Ed Barnes, Ph.D., Program Coordinator, Rocky Mountain Medical Physics, Inc., 6127 W. Lakeside Ct., Littleton, CO 80125, phone (303) 778–1955, ext. 1713.

Information on hotel arrangements may be obtained from Edward S. Sternick, Ph.D., Chairman, Local Arrangements, Tufts-New England Medical Center, Medical Physics Division, 171 Harrison Avenue, Boston, MA 02111, phone (617) 956–6171.

Radionuclides in Nephrology
Fifth International Symposium

September 2–4, 1981, at The Royal Society, London. Further details from A. R. Constable, Institute of Urology, 172 Shaftesbury Avenue, London WC2 8JE. Closing date for abstracts April 20.

Digital Diagnostic Radiology
Nuclear Magnetic Resonance

September 5, 1981. Department of Diagnostic Radiology, University Hospital, Bern, Switzerland. 12th Symposium on actual problems of diagnostic radiology. Guest faculty: P. Capp, Tucson (Arizona), A. B. Crummy, Jr., Madison (Wisconsin), Th. Meany, Cleveland (Ohio), M. Pfeifer, Erlangen (Germany), R. Damidian, Millville (NY), A. Löffler, Erlangen (Germany) and G. N. Holland, Nottingham (UK).

Contrast Media. Fundamentals and Clinical Application

The Department of Diagnostic Radiology of the University of Rochester will offer a two-and-a-half day course on Contrast media: fundamentals and clinical application, September 21–23, 1981. The philosophy of this course is to review the fundamental chemical, physical, physiological, and toxicological properties of radiopaque media and to describe the relationship and importance of these properties to radiological application and diagnoses. The curriculum will provide a thorough introduction to contrast media for residents, Fellows, and junior faculty as well as a refresher course for the more experienced radiologist. The knowledge conveyed should be useful in the clinical setting and in the laboratory. For further information, contact Harry W. Fischer, M.D., Chairman, or Michael R. Violante, Ph.D., Course Director, Department of Radiology, PO Box 648, University of Rochester Medical Center, Rochester, New York 14642; phone (716) 275–2617.

Skeletal Radiology

The Eighth Refresher Course of the International Skeletal Society will be given in Madrid, Spain, September 25–27, 1981.

For further information, please write to: A. Bonakdarpour, M.D., Department of Diagnostic Radiology, Temple University Hospital, 3401 North Broad Street, Philadelphia, PA 19140, USA; or Prof. Dr. Friedrich W. Heuck, Zentrales Röntgeninstitut, Katharinen Hospital der Stadt Stuttgart, Kriegsbergstrasse 60, Stuttgart 1, Germany.

European Association of Radiology
II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

Radiology of the Mediastinum
4th Postgraduate Course in Radiology "P. Perona"

Will be held in Verona, Italy, October 1–3, 1981, organized by the Institute of Radiology of the University of Verona, the Italian Society of Radiology, and the College d'Enseignement Post-Universitaire en Radiologie. Simultaneous English/French translation. Registration L.65000. Information: Radiology Department, University Hospital, Verona (phone 045/582445).

III Meeting of European Hyperthermia Group

The third meeting of the Co-operative European Hyperthermia Group, sponsored by the EORTC, will take place in Rotterdam, Holland, on Friday and Saturday, October 2–3, 1981, in the Rotterdam Radiotherapeutic Institute. The programme will encompass topics on thermobiology, the methodology of heating, and clinical applications and results. For further details, abstract forms and registration, please contact Prof. Dr. H. S. Reinhold, Integraal Kankercentrum Rotterdam, dr. Molewaterplein 50, Rotterdam, Netherlands.

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

Symposium on Education and Training in Radiobiology

Dresden, May 12–15, 1982. Organized by the Gesellschaft für medizinische Radiologie der DDR, under the auspices of the European Society of Radiology. Languages: English, French and German. Registration by December 1, 1981; papers by August 15, 1981. Information: Professor R. Barke, Radiologische Klinik, DDR – 8019, Dresden, Fetscherstrasse 74.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

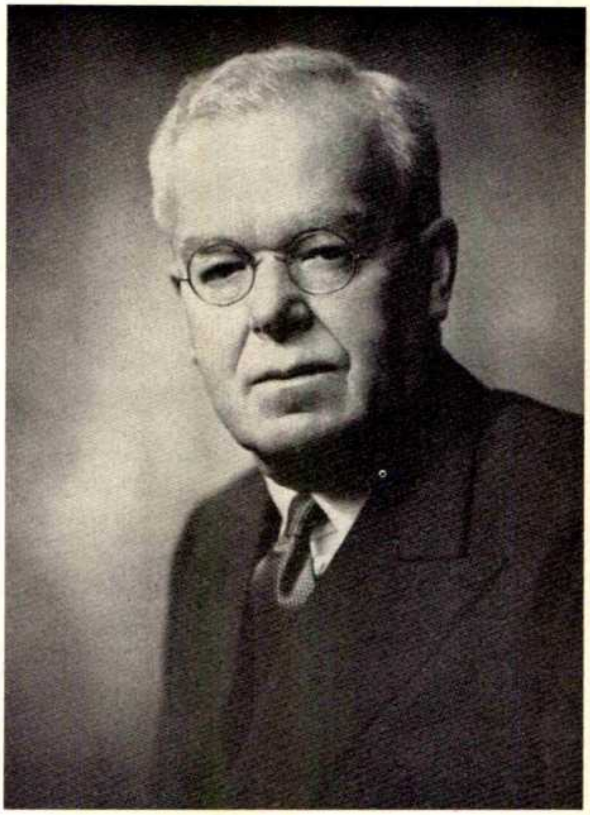
Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01–486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

Obituary

Frederick Gordon Spear, M.D., M.A., M.B., B.Chir., D.M.R.E., F.F.R., D.P.H., D.T.M. & H.



Sylvanus Thompson Memorial Lecturer 1949, Röntgen Prize 1950, Honorary Membership 1956, Mackenzie Davidson Memorial Lecturer 1958, President 1961–62, Barclay Medal 1966. These are the outward signs of a commitment to the Institute that few of its members can have equalled during its history. Gordon Spear was passionately devoted to the concept of the Institute as a truly corporate body, gaining its strength from the friendship and dialogue between its different constituent groups. He worked for this in many ways—the yearly Conversaziones were one of his innovations—but his major contribution lay in the bringing together of the non-medical and medical members through radiobiology. For many of us who joined the Institute as "pure" physicists, he was our guide into biology, and the courses he and Dr. Glucksmann organized at the Strangeways Research Laboratories, Cambridge, where he was Deputy Director, proved very important events in our professional careers. It was most appropriate that he should become a "radiobiological" President of the Institute in 1961–62, and he was not only amused but rather proud of being regarded for the purposes of presidential succession as a "non-medical." He was the obvious person to give the first Douglas Lea Memorial Lecture of the Hospital Physicists' Association in 1949, taking as his subject "The Physicist and his Colleagues". This lecture was given at the Institute and subsequently published in THE BRITISH JOURNAL OF RADIOLOGY, 1950, *23*, 74–82.

Radiation protection was another of his deep concerns, not only as an active participant in the national protection committee but as a historian of its development. Throughout his work on radiation protection he was the biologist, insisting that the essential problem was not the action of penetrating radiation on biological material, but the response of living cells to penetrating radiation. His own research work, much of it done in collaboration with Dr. Glucksmann, was concerned with identifying the more subtle responses of biological material to the particular type of damage produced by radiation, and their significance for therapy and for our understanding of radiation hazard.

He had a great feeling for the history of the Institute, so evident in his Memorial Lectures, and he wrote beautifully. He was a scholar, fascinated with the origin and meanings of words and with a great knowledge of English literature. Perhaps quite appropriately, owls were a hobby of his, and some of us will remember the determination with which he pursued, and succeeded in acquiring, OWL 1 as the registration number of his car.

Gordon Spear was the most delightful of people to meet and know, kind and generous in every way. It will not come as a surprise to learn of the nature of his career before he joined the Strangeways Laboratories. After Cambridge and qualifying at St. Thomas's Hospital (where he wrote a thesis concerned with radiological diagnosis under Dr. Archibald Reid) he studied tropical medicine in London and Belgium and went, at his own expense, to work in a Missionary Hospital in the Belgian Congo, where his sister was already working.

He was married twice but both his wives predeceased him and he had two adopted daughters. He died on September 15th, at the age of 85, after a long illness. We remember him with gratitude and affection.

L. F. LAMERTON.

Book reviews

Quantitative Concepts and Dosimetry in Radiobiology. ICRU Report 30. pp. vii + 71, ill., 1979 (International Commission on Radiation Units and Measurements, Washington DC), $10.00.
ISBN 0–913394–49–1.

This report brings up to date many of the topics covered in an earlier report "Radiobiological Dosimetry" (ICRU Handbook 88, 1963). In addition, it defines and discusses quantitative concepts used in the representation and analysis of radiobiological effects and in the specification of radiation quality. It also covers a number of practical aspects of experimental irradiation, including examples of arrangements for exposure to various particle beams. Overall, the report is a collection of defined concepts, recommendations, dosimetric data and practical know-how that are of considerable value to radiobiologists and others concerned with the application of external sources.

Some of the mathematical properties of the model dose-effect relationships in general use are described and the main concepts used to quantify modification of response are defined. There is a section on the specification of radiation quality in terms of LET, track structure and microdosimetry, then sections on dosimetry and on practical aspects of dose distribution and dose specification. There follow two useful appendices, the first giving well-illustrated examples of correct methods of exposure of specimens to X rays, fast electrons, fast neutrons, π mesons and heavy ions, the second being a glossary of terms and definitions. Throughout, the emphasis is on standardization of terminology and procedures and the report contains many useful data and source references.

B. D. Michael.

Low Back Disability. Neurosurgical, orthopaedic and radiological symposium. Edited by B. R. Selecki. pp. xvii + 198, 1978 (Australasian Medical Publishing Co., Glebe, NSW), $A 25·00.

This is a collection of papers on mechanical disorders of the low back by a group of authors from Sydney, Australia, comprising orthopaedic and neurosurgeons, a neurologist, a pathologist and radiologist. There are eight chapters (195 pages), each complete in itself, forming really a series of short monographs or lectures on the aetiology of low back pain, the biomechanics of disc disease with experimental studies on cadaveric material as well as a discussion of surgical techniques and complications.

One chapter is devoted to the radiological aspects of chronic low back pain, but the author Dr. H. B. L. Williams also contributes to three other multi-author chapters. There are no less than seven forewords, mainly by distinguished surgeons, who congratulate the authors on their achievement in bringing together people of differing disciplines in an attempt to determine the common ground of low back pain as well as stating points where opinions differ. Inevitably there will be sections of the book which will be of interest mainly to the research worker or anatomist but, on the other hand, no radiologist, physician or surgeon could claim any special knowledge in this field unless he were aware of current research and opinion. This book is therefore a "must" for anybody embarking on a study of the mechanisms, investigation and treatment of low back pain. The symposium is well thought out, clearly discussed and has a good list of references.

J. T. Patton.

Books received

Receipt of the following books is acknowledged as a courtesy to the senders. They have been lodged in the Library of The British Institute of Radiology for the use of members.

A Series of Workshops on the Biology of Human Cancer. Report No. 7. Malignant Lymphoma. (UICC Technical Report Series 37). pp. 239, 1978 (International Union against Cancer, Geneva), Sw.Fr. 20.

Traité de Radiodiagnostic. 9. Gynécologie, Obstétrique, Sénologie. By J. Chalut *et al.*, pp. xvii + 644, 1980 (Masson, Paris), n.p.
ISBN 2–225–64691–0

Tomografia computerizzata del Cervallo. Italian text). By G. Ruggiero, L. Sabbatini and G. Scialfa. pp. xi + 672, 572 ill., 1980 (Il Pensiero Scientifico, Rome). L.120 000.

New journal

Nuclear Medicine Communications. Edited by K. E. Britton, P. J. Ell and R. F. Jewkes. Vol. 1, Nos. 1–6, 1980 (Chapman & Hall and The British Nuclear Medicine Society, London). Subscription £20 (UK), £24 (abroad), £26·50 (airmail); single copies £4·50.
ISSN 0143–3636

Correspondence. 364
  Deceptive duodenal deformity.
    I. Beggs
  Isolated dislocation of the pisiform.
    A. Laczay
  Isolated dislocation of the pisiform.
    M. Sundaram
  A new rectal marker for treatment planning.
    M. A. Coe and B. Baily
  Media for single contrast knee arthrography.
    J. D. O'Connell

Proceedings of The British Institute of Radiology. 367
  Radiobiology work-in-progress meeting: radiosensitizers and radioprotectors.
  Whole body irradiation.

Forthcoming events. 373

Obituary. 375
  Frederick Gordon Spear.

Book reviews

The practice of biliary surgery 288
Roentgenologic anatomy 295
Cardiac nuclear medicine 301
ABC Radiodiagnostic. 3 301
Nuclear medicine physic 306
Quality assurance measurements in diagnostic radiology 306
Ultrasound in medicine and biology 311
Manual of ultrasonography 311
Measurement of the performance characteristics of diagnostic X-ray systems 311
Heavy particle radiotherapy 324
Noncoherent optical processing 334
Radiant energy and the eye 334
Reflux nephropathy 366
Perceptions of risk 372
Mathematics for technologists in radiology 372
Quantitative concepts and dosimetry in radiobiology 376
Low back disability 376
Books received 376
New Journal 376

Errata

In the contents list of book reviews in THE BRITISH JOURNAL OF RADIOLOGY for March 1981, the wrong page numbers were given in three cases and one review was omitted from the list. Please correct as below.

Review of medical terminology 231
Practical gastrointestinal endoscopy 244
Encyclopaedia of Medical Radiology. 5, 6. Bone tumors 275
Bone tumors. Diagnosis and treatment 275

VOL 54 NO 640 APRIL 1981

The British Journal of Radiology

Contents

Page

The radiographic detection of acute pulmonary oedema. A comparison of radiographic appearances, densitometry and lung water in dogs. 277
P. D. Snashall, Suzanne J. Keyes, Barbara M. Morgan, R. J. McAnulty, P. F. Mitchell-Heggs, J. M. McIvor and K. A. Howlett

A method of measuring the radio-opacity of catheters. 289
J. C. Gore and G. R. Hooker

Left ventricular segmental wall motion—a comparison between equilibrium radionuclide angiography and contrast angiography. 296
D. N. F. Harris, D. N. Taylor, B. C. Ogilvie, N. W. Garvie, J. Watkins, D. M. Ackery and N. Conway

Comparison of intravenous radionuclide cholescintigraphy and endoscopic retrograde cholangiography in the diagnosis of intrahepatic gall-stones. 302
Miau-Ju Huang, Yun-Fan Liaw and Cheng-Shyong Wu

Ultrasound in hepatoma—can specific diagnosis be made? 307
P. A. Dubbins, D. O'Riordan and W. M. Melia

Management of soft tissue tumours by limited surgery combined with tumour bed irradiation using brachytherapy and supplementary teletherapy. 312
E. E. D. Mills and E. R. Hering

Misonidazole as a radiosensitizer in the radiotherapy of glioblastomas and oesophageal cancer. Pharmacokinetic and clinical studies. 318
P. Tamulevicius, M. Bamberg, E. Scherer and C. Streffer

Indium (^{111}In)-labelled platelets in the diagnosis of renal transplant rejection: preliminary findings. 325
A. Fenech, A. Nicholls and F. W. Smith

Portable transfer digital dosemeter for beam output measurements with X and gamma rays, electrons and neutrons. 328
A. Sankaran, R. S. Gokarn and P. Gangadharan

Ultrasound appearances of liver hydatid disease. 335
E. A. Niron and H. Özer

Case reports. 339
- Encysted peritoneal hydatidosis, unusual ultrasonographic and clinical presentation of liver echinococcosis.
  E. A. Niron, H. Özer and H. Dolunay
- Acetabulum excavatum in adult Down's syndrome.
  G. Evison and Margaret Oliver
- Colonic polyps in an infant following necrotizing enterocolitis.
  C. Dicks-Mireaux, D. G. Shaw and C. Fisher
- Osteopathia striata with sclerosis and thickening of the skull.
  M. R. Paling, I. Hyde and N. R. Dennis
- The fate of valves of autogenous vein grafts.
  P. C. Clifford, J. P. Woodcock and R. N. Baird
- Ultrasonic demonstration of renal artery thrombosis.
  P. Barber-Riley and A. S. Patel
- The role of ^{131}I-19-iodocholesterol scintigraphy and ultrasonography in the localization of a poorly vascularized phaeochromocytoma.
  L. Troncone, P. G. Falappa, A. Cavallaro and G. Netri.

Technical notes. 356
- A hybrid real time/B scan ultrasonic system. Implications for clinical practice based on a two-year experience.
  S. R. Wild, W. A. Copland and W. N. McDicken
- Measurement of chest-wall thickness using a simulator.
  C. F. Westermann and G. Kòk

Short communications. 361
- Radiation survival of glutathione-deficient human fibroblasts in culture.
  P. J. Deschavanne, E. P. Malaise and L. Révész
- Pulmonary metastases from differentiated thyroid carcinoma detected only by radionuclide imaging.
  D. Casara, P. L. Zorat, B. Busnardo and M. E. Girelli

(continued on inside back cover)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
32 Welbeck Street, London W1M 7PG

ISSN 0007-1285
16425

14.9.81

Volume 54 Number 641
May 1981

THE BRITISH JOURNAL OF RADIOLOGY

[illegible]

[illegible]

[illegible]

[illegible]

Radiotherapy

Radiobiology

Radiation protection

and related disciplines

LIBRARY

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01–935 6237 and 01–935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

APPEAL

A permanent home for British radiology

The Appeal Committee

Sir Jan Lewando, CBE (*Chairman*)
Professor G. H. du Boulay (*Appeal Co-Ordinator*)
Mr. L. F. Barr Smith
Dr. Julian Bloom
Sir Richard Doll, OBE, FRS
Mr. Kevin Hughes, OBE
Professor L. F. Lamerton
Sir Thomas Lodge
Dr. J. F. Loutit, CBE, FRS
Professor W. V. Mayneord, CBE, FRS
Professor J. H. Middlemiss, CMG
The Lord Penney, OM, KBE, FRS
Sir Edward E. Pochin, CBE
Sir John Read
Mr. C. F. E. Shakerley
Professor Sir David Smithers
Professor R. E. Steiner, CBE
Dr. Herman D. Suit
Dame Janet Vaughan, FRS
Professor Sir Brian Windeyer
The Lord Zuckerman, OM, KCB, FRS

The President of the Institute and Appeal Executive Committee members

Funds are still needed for the new permanent home for The British Institute of Radiology at 36 Portland Place, London W1, next door to the Royal College of Radiologists

Donations and ideas to:
Appeal Co-Ordinator, 32 Welbeck Street, London W1M 7PG (01–486 5084)

THE FACULTY OF
RADIOLOGISTS
OF
THE ROYAL COLLEGE
OF SURGEONS IN IRELAND

21st
ANNIVERSARY
MEETING
to be held in
DUBLIN
2nd-3rd OCTOBER 1981
with
THE BRITISH INSTITUTE OF
RADIOLOGISTS
ROYAL COLLEGE OF
RADIOLOGISTS
ROYAL SOCIETY OF MEDICINE

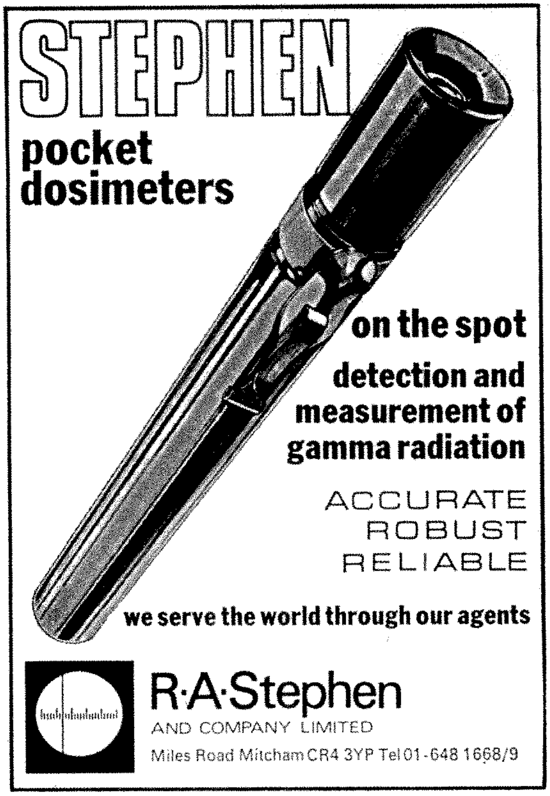
Diagnostic and Therapy Sessions

Topics to include
Radiology in Renal Failure
Radiology of Trauma

Proffered Papers
BIR Presidential Address:
Dr. David Trapnell
"Chest Radiology–Guesswork or
Science"

Technical Exhibition

Further information from
Miss Anne Daly,
Faculty of Radiologists,
Royal College of Surgeons in Ireland,
Stephen's Green, Dublin 2



STEPHEN
pocket
dosimeters

on the spot
detection and
measurement of
gamma radiation

ACCURATE
ROBUST
RELIABLE

we serve the world through our agents

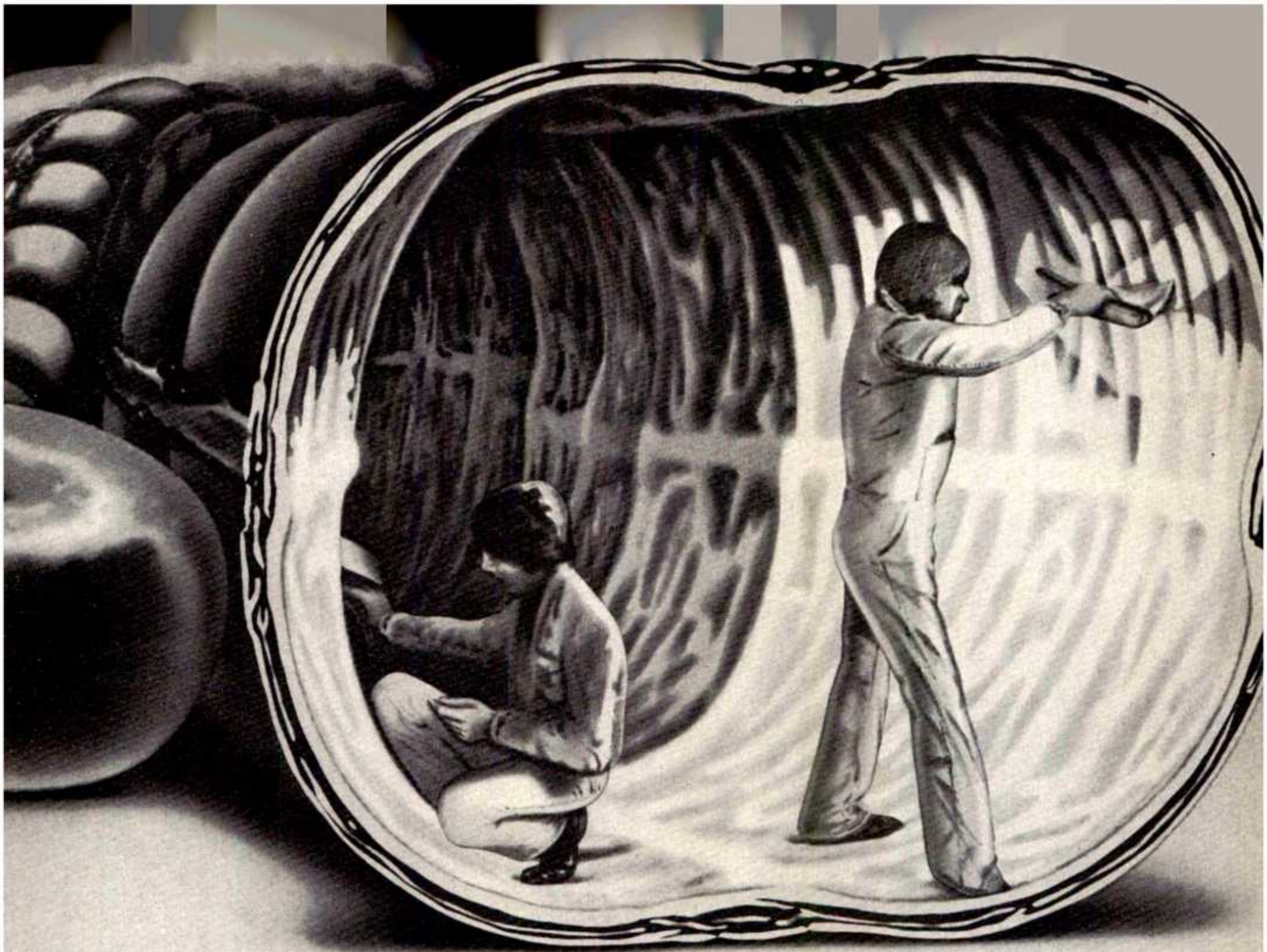
R·A·Stephen
AND COMPANY LIMITED
Miles Road Mitcham CR4 3YP Tel 01-648 1668/9

Computers
Two BIR Special Reports

Considerations about the use of computers in radiodiagnostic departments
BIR Special Report 14
Edited by Professor G. H. du Boulay 1977
SPECIAL PRICE: £1·00

Computers in the control of treatment units
BIR Special Report 16
By a multi-disciplinary task group convened by R. E. Bentley. 1979
PRICE: £2·40

Orders to:
The British Institute of Radiology
32 Welbeck Street
London W1M 7PG
ISSN 0306–2120



baritop ensures smooth and even coating of the GI tract

The high density, low viscosity and ultra-fine particle size of Baritop allows optimum visualisation of the areae gastricae and the innominate grooves. Baritop consistently gives excellent resolution.

Baritop 100 is a ready made suspension supplied in a ring-pull can for easy use. If you prefer a higher density use Baritop G powder.

Baritop makes the most of your double contrast technique.

Concept Pharmaceuticals Ltd.,
Russell House, 59-61 High Street, Rickmansworth WD3 1EZ
Tel: Rickmansworth (092 37) 79388/9/0 Telex: 925794

baritop

for those who seek perfection

SKIASKANS **THE REDUCTION OF RADIOGRAPHS TO 35mm.**

- New Technology with the **SCANATRON 35**
- Total Image Reproduction
- Full or Partial Bureau Service
- Quality Control

medical illustration support service. ltd.
The Royal College of Surgeons of England
35-43 Lincoln's Inn Fields London WC2 3PN
Telephone : 01 404 4141

RADIATION PROTECTION of the PATIENT

A Manual of Good Practice

Edited by : Walter A. Langmead

Part I. — Diagnostic Radiology

Price £2.95

This Manual is concerned with the radiation protection of patients undergoing diagnostic examinations or treatment with ionising radiations. It examines the responsibilities of the many individuals — general practitioners, clinicians, radiologists, radiographers and physicists — whose special fields of knowledge together contribute to the radiation safety of the patient, and it proffers advice to each in turn as to the preferred procedures to minimise the patient's radiation dose without reducing the level of diagnostic achievement or the efficacy of treatment.

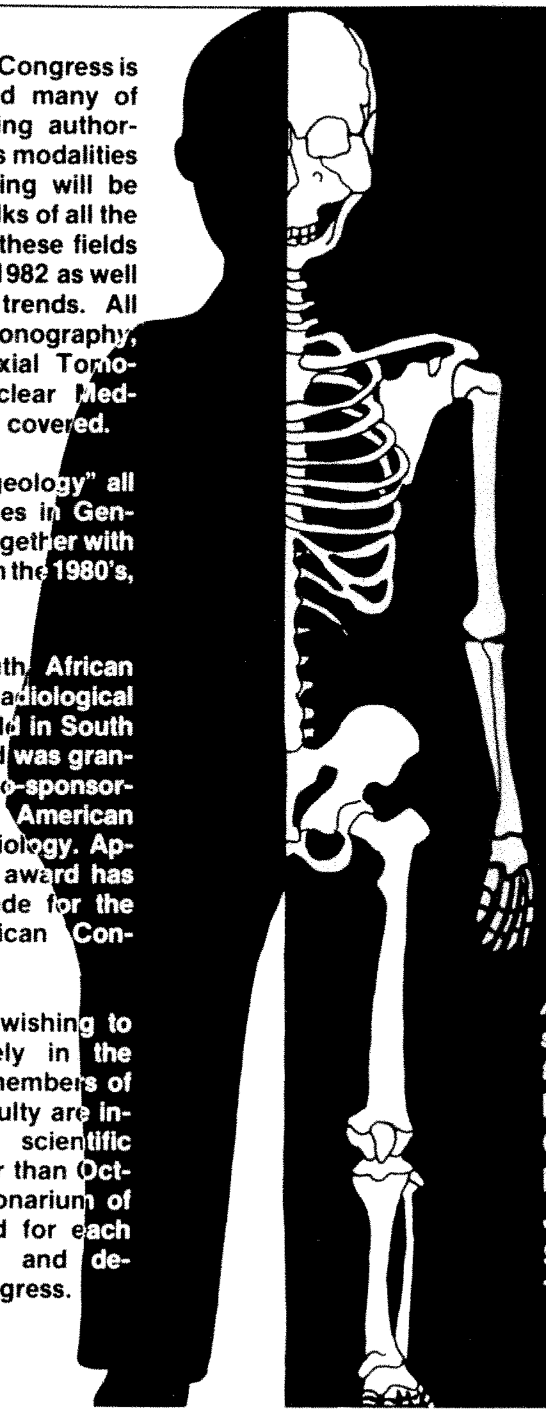
The Manual is to be published in three Parts, dealing respectively with radiology, nuclear medicine and radiotherapy. PART I. — DIAGNOSTIC RADIOLOGY, covers the X-ray examination from the initial request to the final report. The scientific and technical factors which enable the clinical objectives to be attained with minimal dose to the patient are also reviewed. Two Appendices give recommendations respectively for certain specialised X-ray examinations, and for a departmental guide to radiographic procedures.

The benefits of medical diagnosis and treatment with radiation are large, and the potential radiation hazards arising therefrom are comparatively minor in most cases. Nevertheless, the safety of the patient is paramount and this results from good teamwork and attention to detail, as outlined in this Manual.

Prepared by Panels of the British Radiological Protection Association; and published by the British Institute of Radiology.

Orders to BIR Publications, 32 Welbeck Street, London W1M 7PG (01-935 6867)

FIFTH SOUTH AFRICAN INTERNATIONAL RADIOLOGICAL CONGRESS
"IMAGEOLOGY 1982"
OCTOBER 8 — 15TH 1982.



The theme of the Congress is "Imageology" and many of the world's leading authorities in the various modalities of medical imaging will be giving detailed talks of all the developments in these fields prior to October 1982 as well as their future trends. All aspects of Ultrasonography, Computerised Axial Tomography and Nuclear Medicine will be fully covered.

Apart from "Imageology" all the latest advances in General Radiology, together with its future course in the 1980's, will be discussed.

The Fourth South African International Radiological Congress was held in South Africa in 1978 and was granted a Credit 1 co-sponsorship by the American College of Radiology. Application for this award has already been made for the Fifth South African Congress in 1982.

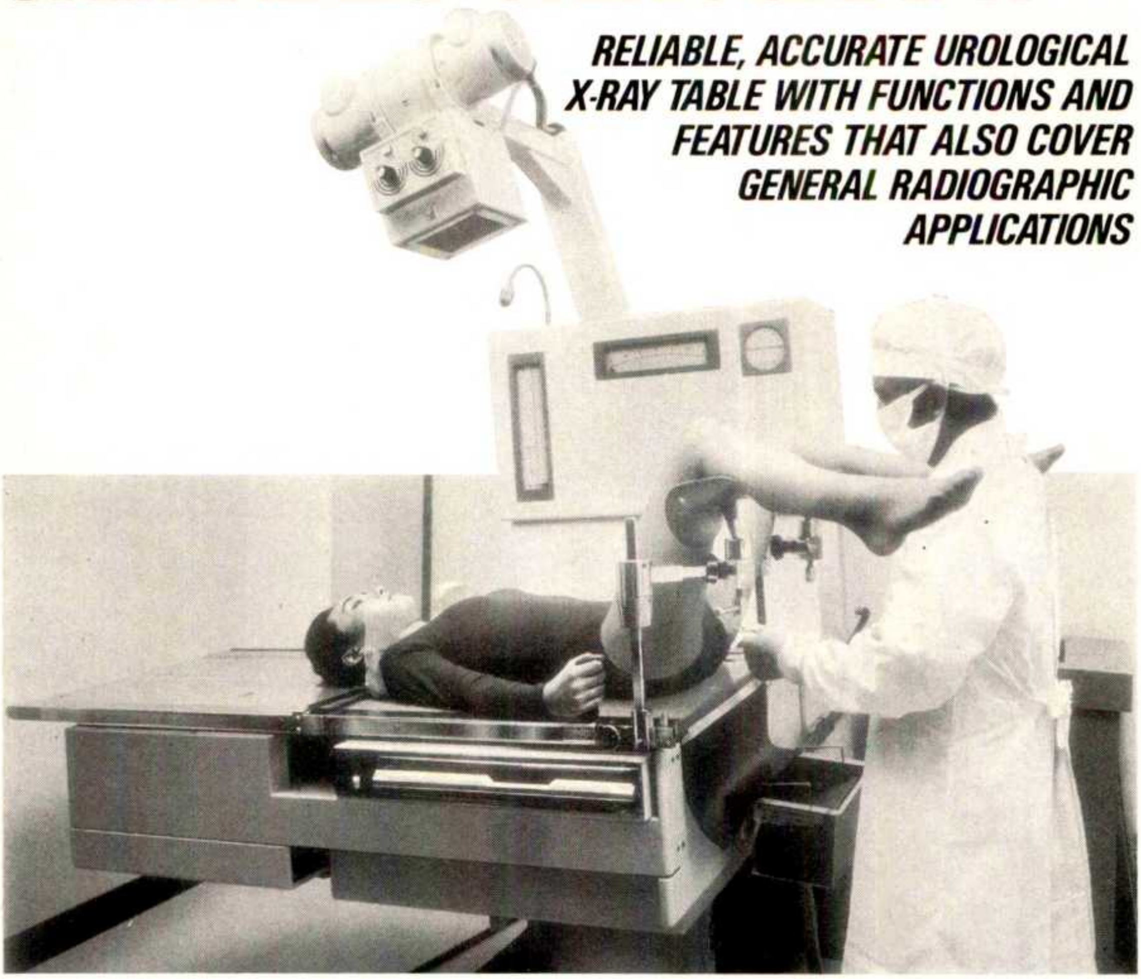
Those delegates wishing to participate actively in the programme as members of the Overseas Faculty are invited to submit scientific papers by no later than October 1981. An Honarium of $250 will be paid for each lecture accepted and delivered at the Congress.

South Africa as a country is a world in one so why not take this opportunity of spending part of October, the loveliest of our Spring months, in Johannesburg, the modern 'city of gold' which grew out of the old mining camp of the 1880's. Take advantage of our organised tours to visit the famous winelands of the Cape, the ostrich farms and the mother city herself, historic Cape Town with its famous Table Mountain. Alternatively, stay in the tranquility of the Kruger National Park in the heart of the African bush and watch elephant and lion come down to the waterholes in the cool of the tropical evening.

All further inquiries should be forwarded to the Congress Director.

Dr. Pete Reichman
Congress Organiser
PO Box 2251
Johannesburg
South Africa 2000
Tel. (011) 37-6060

SHIMADZU URINOGRAPH



RELIABLE, ACCURATE UROLOGICAL X-RAY TABLE WITH FUNCTIONS AND FEATURES THAT ALSO COVER GENERAL RADIOGRAPHIC APPLICATIONS

The **URINOGRAPH** is an examination table that not only permits transurethral surgery, endoscope examination, and other routine tasks performed in urology and gynecology without resorting to X-ray examination, but also allows X-ray examination in combination with such medical treatment programs.
Besides ordinary radiography, the **URINOGRAPH** also permits TV fluoroscopy, spotfilming, oblique beam technique and tomography. Dose saving in fluorography through the use of an image amplifier is of particular importance in urology.

See SHIMADZU at
the ICR-81, Brussels, June, 1981
Booth No. **9203 & 9302**

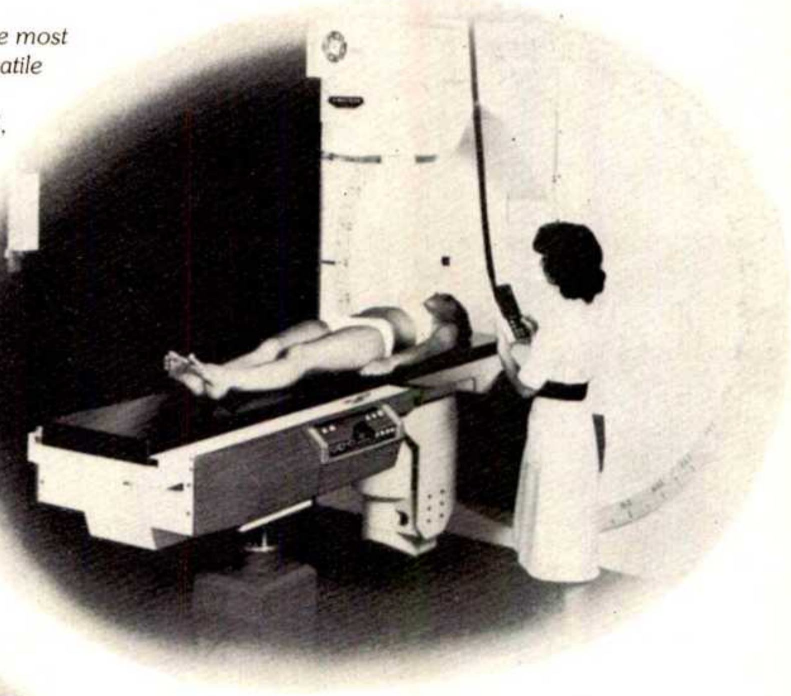
SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Düsseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

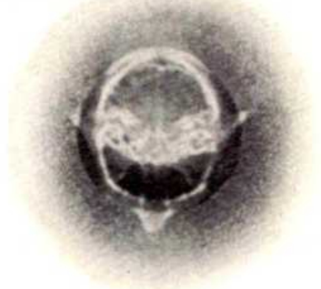
TEM

Ximatron 5
Treatment Planning Simulator

The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.

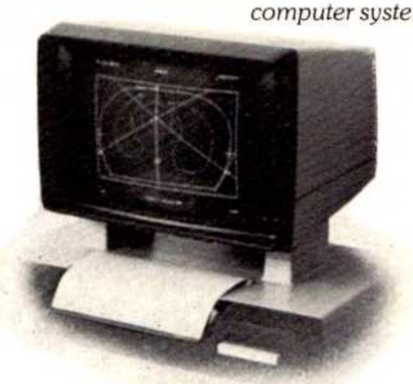


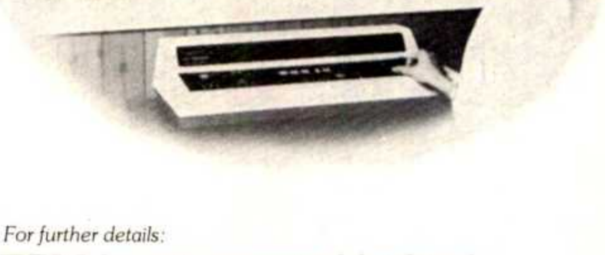
Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.

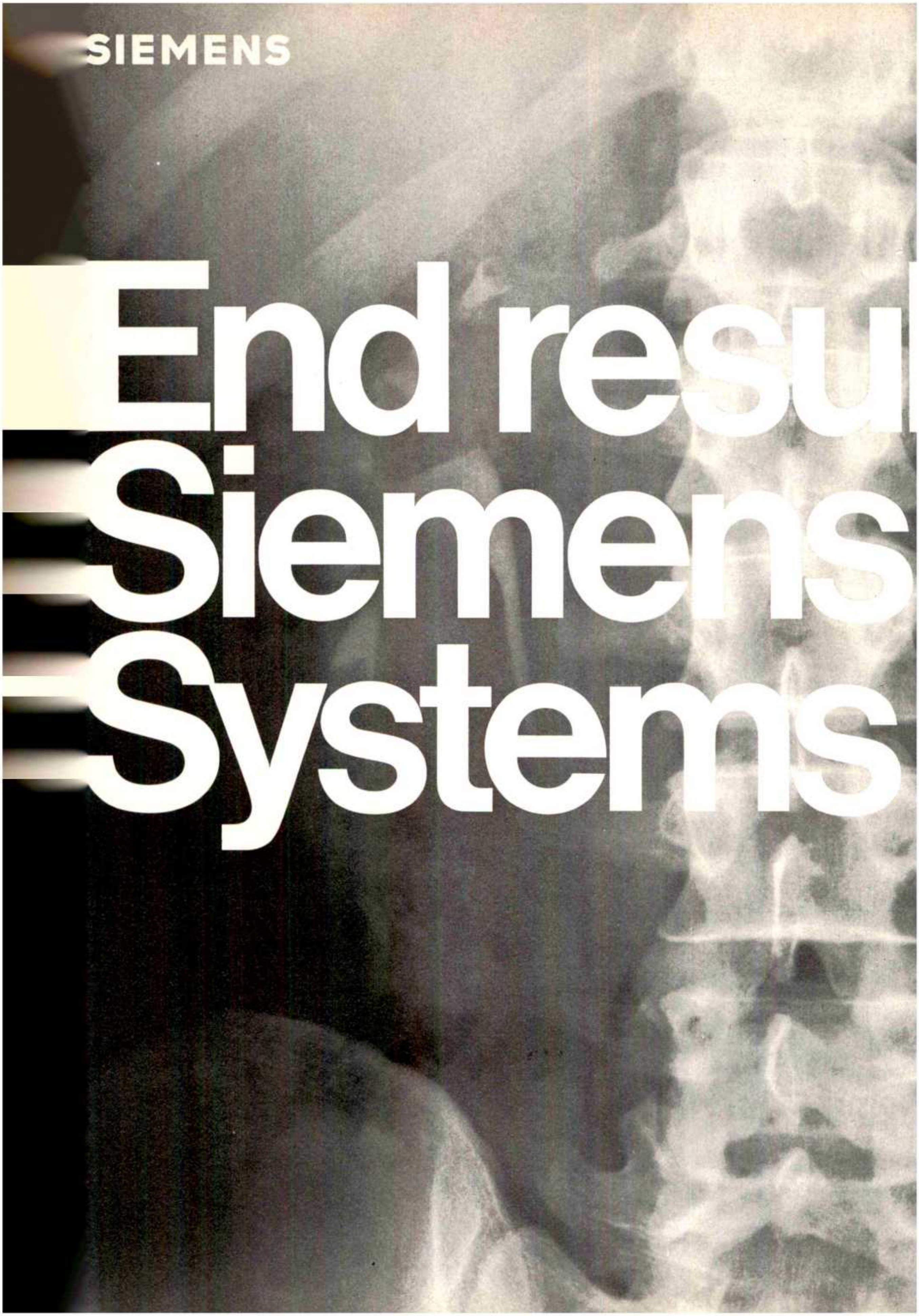
The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.

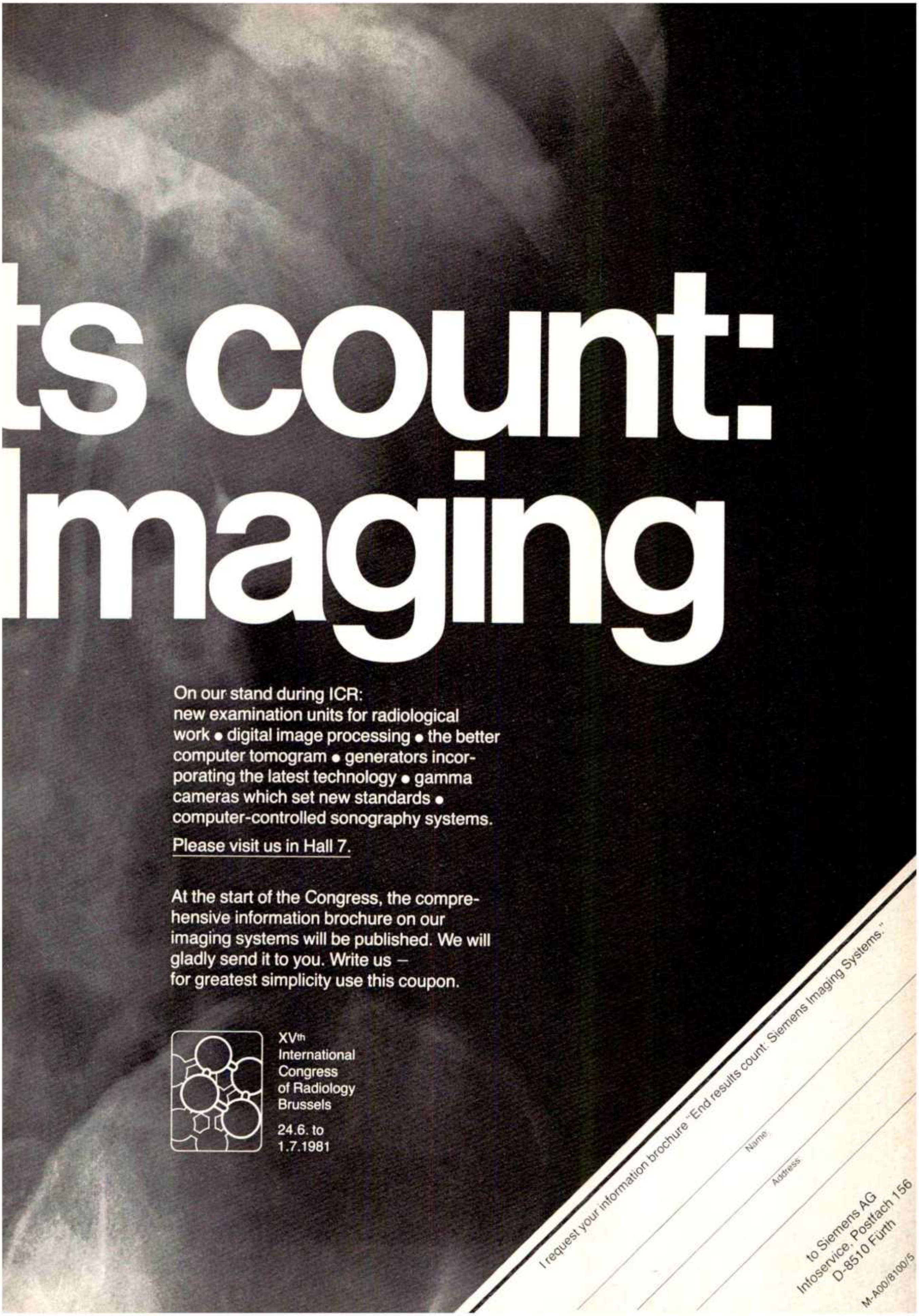




For further details:

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY


SIEMENS
End resul
Siemens
Systems


ts count:
Imaging

On our stand during ICR:
new examination units for radiological work • digital image processing • the better computer tomogram • generators incorporating the latest technology • gamma cameras which set new standards • computer-controlled sonography systems.

Please visit us in Hall 7.

At the start of the Congress, the comprehensive information brochure on our imaging systems will be published. We will gladly send it to you. Write us – for greatest simplicity use this coupon.

XV^th^ International Congress of Radiology Brussels

24.6. to 1.7.1981

I request your information brochure "End results count: Siemens Imaging Systems."

Name

Address

to Siemens AG
Infoservice, Postfach 156
D-8510 Fürth

M-A00/8100/5

See X-Rays in a new light.

J.K. LIGHTING have developed a special range of X-ray viewing light box's, together with an executive light case. Both of special interest to both doctors + dentists alike. Send this coupon now for our leaflet and price list."

Tudor Works, Beaconsfield Road,
Hayes, Middlesex. Tel: 01-848 3661/2

JENRICK

Please send me your full colour brochure. J K Lighting Displays Ltd.
Tudor Works, Beaconsfield Road, Hayes, Middlesex. Tel: 01-848 3661/2
Name ....
Address ....

J. K. Lighting Displays Ltd.

The London Ultrasound Course for Radiologists

October 19th–23rd 1981

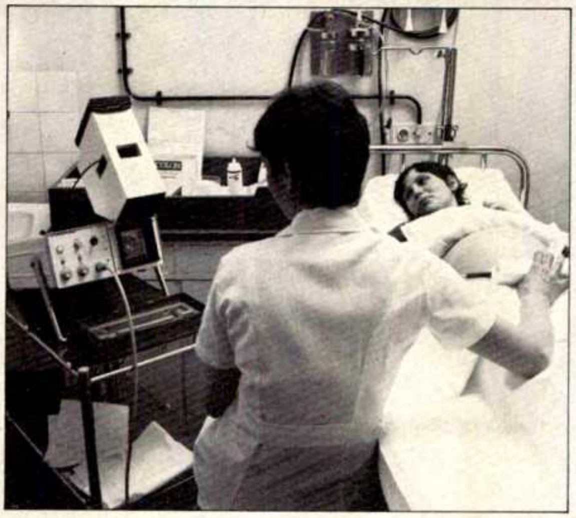
This course in clinical ultrasound is designed to cover non-obstetric abdominal scanning in depth, but will also include certain other applications. The course will be held in a London hotel and will be limited to 50 participants.

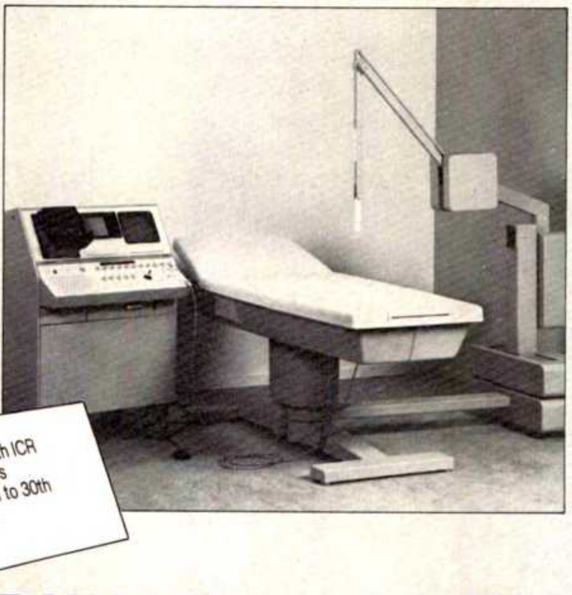
Course leaders:–
David Cosgrove Keith Dewbury Hylton Meire
Further information from:–
Dr. H. B. Meire, Clinical Research Centre, Harrow, Middlesex
HA1 3UJ
UK

IT'S YOUR RESULTS THAT MATTER.

In ultrasound diagnosis.

Since today ultrasound is firmly established as a first order diagnostic method, more attention is concentrated on image quality and application flexibility.
Anticipating this, we developed a range of ultrasonic systems to ensure a high standard of diagnostic confidence.
To achieve superior image quality we employed new techniques and digital pre- and post-processing including digital scan conversion. Special transducers such as the new servo sector ensure clear signal input.
You can see the difference. And you can select a system perfectly adapted to your diagnostic needs.
This applies to the truly portable (8.8 kg) real-time Sono DIAGNOST R1000 that permits examinations where and when needed without delay.
It applies as well to the universal self-contained scanning systems of the Sono DIAGNOST B7000 series, covering the entire spectrum of ultrasonic examination and diagnosis.
They comprise A-mode, B-scan, M-mode and real-time. These systems are truly modular and can easily be adapted to your special requirements.
The compact console is ergonomically designed for effortless operation. A wide choice of scanning arms, transducers and examination tables corresponds with clinical requirements.
Many special features such as the unique hand controller facilitate and speed the examinations.
When you work with one of these systems and see how fast and efficiently diagnostic results are obtained you know what we mean by a high standard of diagnostic confidence.
To get full details about the Sono DIAGNOST systems please mail the coupon.*
Philips Medical Systems cover the range of advanced diagnostic imaging and radiation therapy.





See us at the 15th ICR
at Brussels
from June 24th to 30th
1981.

PHILIPS

Medical Systems

* UK enquiries: Philips Medical Systems, Kelvin House
63/75 Glenthorne Road, Hammersmith, London W6 OLJ.

I want INFORMATION about
Sono DIAGNOST systems

Philips Industries
Systems Division-QM
Communicatio
ndhoven,
nds B

When you need to know the inside story, the Hitachi EUB-22 is a must.

More accurate clinical information is now available faster, thanks to Hitachi technology in this new real time ultrasound system.

The compact lightweight transducer provides access to all areas of interest making the TOMOSONIC EUB-22 ideal for abdominal, obstetric and neonatal imaging.

Dual image display allows expanded field of view or display of side-by-side images either in real time or freeze frame modes, with on-screen measurements.

Superb noise-free, high resolution images produced by advanced digital scan processing and transducer focussing techniques are displayed on the TV monitors. To facilitate the evaluation of those images the TOMOSONIC system provides an exclusive graphics display.

The patient's position during imaging is clearly displayed along with such valuable information as transducer position, patient I.D. date and gain.

SONOTRON MEDICAL ELECTRONICS

SONOTRON LIMITED 29 MIDLAND ROAD, BEDFORD MK40 1PL ENGLAND TELEPHONE: BEDFORD (0234) 40881

also in: AUSTRIA-(02236) 86945 BELGIUM-(02) 7213424 GERMANY-(098) 3205051 FRANCE-(06) 9286945 SWEDEN-(040) 77585
or contact EUROPEAN HEADQUARTERS: SONOTRON AG NEUGASSE 247 P.O. BOX 353 CH 8031 ZURICH, SWITZERLAND TEL: 41-1-425841

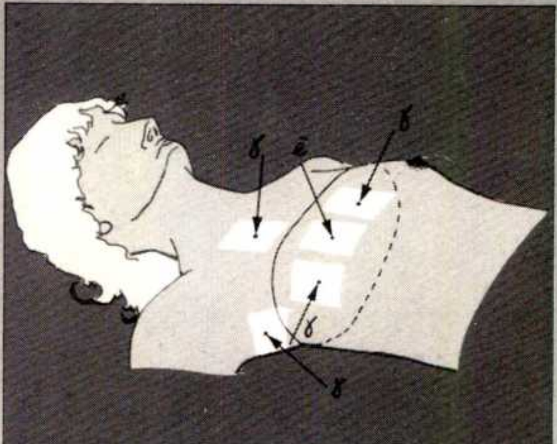
IT'S YOUR RESULTS THAT MATTER.

In planning and documenting radiation therapy.

The results of radiation therapy are inseparably linked to the precision and effectiveness of the treatment planning system. It is the crucial step between diagnosis and therapy.

The very best solution is the integration of CT-scanning results with three-dimensional treatment planning.

Therefore we have developed the new ONCOLOGY SUPPORT SYSTEM. It links up directly with any CT-scanner that produces data in standard format. The direct introduction of patient data, diagnostic results and tumour localization into an advanced treatment planning process offers great advantages to radiation therapy. In addition this system permits statistical evaluation of the recorded tumour data, applied doses and treatment technique as a basis for long-term department planning.



Three-dimensional planning

The ONCOLOGY SUPPORT SYSTEM can also be applied when patients have not been CT-scanned. In this case the patient data are entered graphically.

Ergonomic design of all system components permits easy efficient operation. Planning and evaluation procedures are facilitated by comprehensive software.

The new system is of course fully compatible with the VERICORD SYSTEM for Verification and Recording of treatment parameters.

To get full details about the ONCOLOGY SUPPORT SYSTEM and VERICORD SYSTEM please mail the coupon.

Philips Medical Systems cover the range of advanced diagnostic imaging and radiation therapy.

PHILIPS

Medical Systems

I want information about
ONCOLOGY SUPPORT SYSTEM ○ VERICORD SYSTEM
e
pital
et
n
ntry

Philips Industries
ical Systems Division-QM.
keting Communications
nt., Eindhoven, the
Netherlands.
BJR

Research & development

GUERBET

Better contrast media through research

Laboratoire GUERBET
16-24, rue Jean Chaptal - 93609 Aulnay-sous-Bois - Cedex FRANCE
Tél.: 929.78.37 - Télex: 212382 F.

1981, *British Journal of Radiology*, *54*, 377–380

VOLUME 54 NUMBER 641 MAY 1981

The British Journal of Radiology

Conversion to SI units in radiology

This contribution emanates from the BIR Working Party on SI Units, set up by the BIR Radiological Physics Committee, with members drawn from the following interested bodies: The British Institute of Radiology, the Royal College of Radiologists, the Hospital Physicists' Association, The College of Radiographers, the National Physical Laboratory, together with an observer from the Department of Health and Social Security.

Following the introduction of the International System of Units, SI, by the relevant national and international bodies, the use of this system is now becoming widespread in radiology. In order to facilitate the introduction of this system and to minimize any risk of error, the following tables have been prepared giving conversion factors between the new SI and the old special units that are needed for use with radiological quantities. In addition, some notes regarding multiplying prefixes and the choice of working units for specific applications, as well as a brief bibliography, are appended.

The definition of quantities for use in the measurement of ionizing radiations and radioactivity is the responsibility of the International Commission on Radiation Units and Measurements, ICRU. A *quantity* "characterizes a physical phenomenon in terms that are suitable for numerical specification", for example time and length. A *unit* is a "selected reference sample of a quantity", second and metre being respectively units appropriate to the quantities given as examples above. International responsibility for the definition and selection of units is vested with the General Conference on Weights and Measures (CGPM), who at the request of ICRU approved new named SI units for use in radiology.

BASIC RELATIONSHIPS

Table I, derived from ICRU Report 33, provides the numerical relationships between the old and new units for the principal quantities in general use.

It will be noted that both the quantities absorbed dose and kerma are included in Table I. For those less familiar with the quantity kerma, this is an acronym for "Kinetic Energy Released per unit MAss". It relates to the first stage in the transfer of energy to matter by uncharged ionizing particles, such as photons or neutrons, namely to the kinetic energy of the charged particles released. In the second stage, these charged particles impart energy to matter as the absorbed dose. Equality of absorbed dose and kerma is approached to the degree that charged particle equilibrium obtains and bremsstrahlung production is negligible.

However, it is not the purpose of this contribution to discuss the merits of the respective quantities for

TABLE I

Quantity	Old special unit (symbol)	SI Unit	Special name (symbol)	Relationship*
Exposure	röntgen (R)	$C\,kg^{-1}$	—	$1\,R = 258 \times 10^{-6}\,C\,kg^{-1}$ $1\,C\,kg^{-1} \approx 3.876 \times 10^{3}\,R$
Absorbed dose Kerma	rad (rad)	$J\,kg^{-1}$	gray (Gy)	1 rad = 0.01 Gy 1 Gy = 100 rad
Dose equivalent	rem (rem)	$J\,kg^{-1}$	sievert (Sv)	1 rem = 0.01 Sv 1 Sv = 100 rem
Activity	curie (Ci)	s^{-1}	becquerel (Bq)	$1\,Ci = 37 \times 10^{9}\,Bq$ $1\,Bq \approx 27.03 \times 10^{-12}\,Ci$

*An exact relationship (defined by ICRU) is shown "=", whereas an approximate relationship is indicated by "≈".

TABLE II

Factor	10^1	10^2	10^3	10^6	10^9	10^{12}	10^{15}	10^{18}
Prefix	deca	hecto	kilo	mega	giga	tera	peta	exa
Symbol	da	h	k	M	G	T	P	E
Factor	10^{-1}	10^{-2}	10^{-3}	10^{-6}	10^{-9}	10^{-12}	10^{-15}	10^{-18}
Prefix	deci	centi	milli	micro	nano	pico	femto	atto
Symbol	d	c	m	μ	n	p	f	a

various applications in the field. Such matters have been considered elsewhere. For example, an introductory article relating to both quantities and units in radiology, prepared by W. A. Jennings at the request of the BIR Working Party on SI Units, was published in the June 1980 issue of the BIR Bulletin (vol. VI, No. 2, p. 4). In view of its relevance in providing additional background information to the present contribution, this Bulletin article has been reprinted in this issue of the Journal. In respect of radiotherapy, a memorandum prepared by the British Committee on Radiation Units and Measurements, BCRU, should be consulted (*British Journal of Radiology*, 1980, *53*, 917). The present paper is concerned essentially with conversion factors, including the use of the prefixes introduced by CGPM for general use with SI units.

Use of Prefixes

The available prefixes are given in Table II.

It should be noted that only one prefix may be used at a time with each unit, *e.g.* kilomegabecquerel is not permitted. However, more than one prefix may be used in expressions containing several units, *e.g.* a radionuclide concentration may be expressed in megabecquerels per millilitre, MBq/ml, especially if the respective prefixes result in convenient values for quantities normally encountered in practice. Moreover, it may sometimes be preferable to retain the use of a single prefix over a range in excess of 10^3, in the interests of simplicity and visualization of relative magnitudes (see section on "activity" below).

Rate Quantities

The SI unit of time is the second (s), and this can be used with the prefixes in Table II, *e.g.* millisecond. However, in view of the long-standing and widespread use of the minute (min), hour (h), and day (d), defined in terms of the second, these three units have been approved by the CGPM for use with SI, though they are not coherent with SI.

Tables of Conversions* and Notes Regarding Working Units

The following tables give conversions for a range of multiples of units listed in Table I, employing the prefixes listed in Table II.

(A) *Units for the quantities exposure, absorbed dose, kerma and dose equivalent*

TABLE III

Conversions for units of exposure

1 μR = 258 pC kg^{-1}	1 μC kg^{-1} $\approx$ 3.876 mR
1 mR = 258 nC kg^{-1}	1 mC kg^{-1} $\approx$ 3.876 R
1 R = 258 μC kg^{-1}	1 C kg^{-1} $\approx$ 3.876 kR
1 kR = 258 mC kg^{-1}	1 kC kg^{-1} $\approx$ 3.876 MR

Also: 1 C kg^{-1} = 3876 R
and 1 R = 0.258 mC kg^{-1}.

TABLE IV

Conversions for units of absorbed dose and kerma

1 mrad = 10 μGy	1 μGy = 100 μrad
1 rad = 10 mGy	1 mGy = 100 mrad
1 krad = 10 Gy	1 Gy = 100 rad
1 Mrad = 10 kGy	1 kGy = 100 krad

Also: 1 cGy = 1 rad.

TABLE V

Conversions for units of dose equivalent

1 μrem = 10 nSv	1 μSv = 100 μrem
1 mrem = 10 μSv	1 mSv = 100 mrem
1 rem = 10 mSv	1 Sv = 100 rem
1 krem = 10 Sv	

Note: Sv/Gy = rem/rad

---

*For ease of reference, The British Institute of Radiology is preparing a card summarizing some useful conversion factors which will shortly be distributed free to members (orders accepted from non-members).

TABLE VI

Quantity	Medium	Radiation for which quantity is defined	Unit	Use/limitation
Exposure	air only	photons	C kg^{-1}	Can specify radiation beam
Kerma	*e.g.* any of: air water tissue graphite	only uncharged ionizing particles: photons neutrons	Gy	
Absorbed dose		all ionizing particles: photons neutrons electrons, etc.		Desired physical end-point. Depends on reference conditions

Notes regarding the above quantities

Table VI draws attention to some of the uses and limitations of these quantities.

Notes regarding working units for these quantities

Working units should provide for convenient numerical values in relation to common usage. In summarizing such units for various fields of application, it is necessary to make reference to the alternative quantities available.

The conversion factors resulting from the adoption of coulombs per kilogram, C kg^{-1}, as the working unit for the measurement of *exposure* may be inconvenient. It may be preferable to use air kerma, as this can be expressed in grays, the same unit as for absorbed dose. For photon energies lower than those of ^{60}Co γ rays, an exposure of 1 R is approximately equivalent to an air kerma of 0.87 rad, equal to 8.7 mGy. Conversely, an air kerma of 1 Gy, equal to 100 rad, is approximately equivalent to an exposure of 115 R, or 29.6 mC kg^{-1}. For *diagnostic* radiology, and in other cases where secondary electron equilibrium may be assumed to exist and bremsstrahlung production by the secondary electrons is negligible, air kerma is numerically equal to absorbed dose to air, both expressed in grays.

In regard to *gamma-teletherapy units*, source outputs may be expressed in terms of air-kerma-rate, and Gy min^{-1} at 1 m gives convenient numerical values. For example, a 200 TBq (5.4 kCi) ^{60}Co source would produce an air kerma-rate of about 1 Gy min^{-1} at 1 m. Alternatively, the latter can be expressed as 17 mGy s^{-1}.

For *radiotherapy*, the relevant quantity is absorbed dose to water, and the unit of choice is the gray. However, SI does not prohibit the use of the centigray, cGy, equal to 1 rad, with a view to obviating any change in the former numerical values.

For *radiation processing*, *e.g.* the sterilization of medical products, the quantity of interest is absorbed dose to the irradiated material. Since dose levels commonly used lie in the range 1 to 10 Mrad, the equivalent range of 10 to 100 kGy makes the kilogray the convenient working unit in this field.

The position in respect of *radiation protection* quantities is still subject to international discussions; however, it is anticipated that a quantity derived from dose equivalent will be accepted, which can be expressed in sieverts. In practice, both mSv and μSv may be appropriate as working units under different circumstances.

The position in respect of working units for *brachytherapy* is also subject to international discussion, and no recommendations are made here.

(B) *Units for use with the activity of a radionuclide*

TABLE VII

CONVERSIONS FOR UNITS OF ACTIVITY

1 pCi = 37 mBq	1 Bq ≈ 27.03 pCi
1 nCi = 37 Bq	1 kBq ≈ 27.03 nCi
1 μCi = 37 kBq	1 MBq ≈ 27.03 μCi
1 mCi = 37 MBq	1 GBq ≈ 27.03 mCi
1 Ci = 37 GBq	1 TBq ≈ 27.03 Ci
1 kCi = 37 TBq	1 PBq ≈ 27.03 kCi
1 MCi = 37 PBq	

Notes on working units

There are advantages in restricting the number of prefixes in routine use, and rounding should be in terms of new units.

1. *For internal administration and external application:*

The great majority of amounts of activity administered lie in the range 0.2 μCi to 100 mCi, and this may be converted (after rounding) to 0.01 MBq to 4000 MBq. The use of only one prefix, mega, throughout the range may be preferable to changing from kBq at the lower end of the range to GBq at the upper end.

TABLE VIII

Conversion to rounded numbers in MBq

microcuries (μCi)	0.27	0.54	1.4	2.7	5.4	14	27	54	140	270	540
megabecquerels (MBq)	0.01	0.02	0.05	0.1	0.2	0.5	1	2	5	10	20
millicuries (mCi)	0.54	1.4	2.7	5.4	14	27	54	140			
megabecquerels (MBq)	20	50	100	200	500	1000	2000	5000			

2. *For teletherapy sources*

In this instance, the most convenient prefix is tera, T.

REFERENCES

(i) *Definitive reference on radiation quantities*

Radiation Quantities and Units. International Commission of Radiation Units and Measurements, 1980. ICRU Report 33, (ICRU Publications, Box 30165, Washington DC, USA.)

(ii) *Definitive reference on radiation units*

Le Système International d'Unités (SI). Bureau International des Poids et Mesures, Sèvres, France; translated into English as *The International System of Units (SI)*, National Physical Laboratory, 1980. (HMSO, London).

(iii) *General references on the quantities and units*

Changing to the Metric System: Conversion factors, symbols and definitions. P. Anderton and P. H. Bigg, National Physical Laboratory. Fifth Edition, 1980. (HMSO, London)

Units of Measurement. ISO Standards Handbook 2, 1979, (ISO Central Secretariat, CP56, Geneva 20, Switzerland).

How to write Metric. A style guide for teaching and using SI units. Metrication Board, 1977. (HMSO, London).

(iv) *References relating to the introduction of SI units in radiology*

EEC Council Directive, 80/181/EEC, of 20 December 1979 on the approximation of the laws of the Member States relating to units of measurement and on the repeal of Directive 71/354/EEC, 1980 (Official Journal of the European Communities, L39/p. 40).

Weights and Measures: The Units of Measurement Regulations, Statutory Instrument, 1980, No. 1070. (HMSO, London).

Recommendations on the Introduction of the new SI units for use with Radioactivity and Ionizing Radiations. British Committee on Radiation Units and Measurements. 1978. (National Physical Laboratory, Teddington, Middlesex).

Use of SI units of radiation in the Journal, (Editorial), 1979, *British Journal of Radiology, 52,* 1.

(v) *Two recent books on radiology which use SI units*

Fundamentals of Radiation Dosimetry. J. R. Greening, 1981, (Adam Hilger, Bristol.)

Radioactivity and its Measurement. W. B. Mann, R. L. Ayres and S. B. Garfinkel, 2nd edition (SI units). 1980 (Pergamon International Library of Science and Technology).

TABLE IX

Conversion to rounded numbers in TBq

kilocuries (kCi)	1.4	2.7	4.1	5.4	6.8	8.1	9.5	11	12
terabecquerels (TBq)	50	100	150	200	250	300	350	400	450

Book review

Radiation Quantities and Units (ICRU Report 33). pp. v+25, 1980. (W. R. Ney and ICRU, Washington D.C.). $8.50.
ISBN 0–913394–27–0

This report updates ICRU Report 19 in the light of more recent developments such as the introduction of the gray, the becquerel and the sievert. It is divided into two sections, the first dealing with quantities and units for general use, the second with quantities and units for use in radiation protection.

A short definition is provided of each quantity followed by an explanatory note, the appropriate SI unit and, where applicable, its special name. When a special unit, such as the rad, has been used for a quantity, this in indicated together with its relationship to the corresponding SI unit, but making clear that the special unit is only to be used temporarily and should be gradually abandoned over a period extending to 1985. The quantities and units considered cover the whole field of radiometry, interaction coefficients, dosimetry, radioactivity and radiation protection.

The report will be an essential reference for all workers professionally concerned with radiation, and, since its contents are presented in a clear and readable form, it will be of value not only to the person wishing to understand the exact meaning of *dose equivalent index*, but also to someone who is still not very clear about the subtle difference between a special *name* and a special *unit*.

J. L. Haybittle.

1981, *British Journal of Radiology*, *54*, 381–383

MAY 1981

How much do you know about quantities and units?

By W. A. Jennings

National Physical Laboratory, Teddington, Middlesex

Editor's note

The following introductory article, written at the request of the BIR Working Party on SI Units, was published in the June 1980 issue of the BIR Bulletin (Jennings, 1980). In view of its relevance in providing additional background information to the previous contribution "Conversion to SI units in radiology", this article has been reprinted (with minor amendments) below.

The need for guidance

Evidence of the need for clarification in the use of quantities and units can best be illustrated by quotations from the literature. The following will serve as an example: "primary standard dosimetry laboratories do not calibrate instruments in kerma, as it is not an SI unit." True, kerma is not an SI unit; indeed, it is not a unit at all, but a quantity. However, as a quantity, it can be expressed as the product of a numerical value and a unit—including an SI unit, and one with a special name, the gray.

Let us try to clarify the meaning of the relevant terminology with particular reference to radiation measurement, and then discuss how the introduction of SI units has brought into focus certain problems relating to the choice of the quantities themselves, problems which will be further discussed elsewhere.

Who is responsible for defining quantities and units in radiology?

Firstly, it is important to distinguish between a quantity and a unit. In everyday language, the word quantity means an *amount*, but in the field of measurement, or "metrology", the word *quantity* has a different meaning, namely "to characterize a physical phenomenon in terms that are suitable for numerical specification", such as length, time or absorbed dose (of radiation). On the other hand, a *unit* is a selected reference sample (or dollop!) of a quantity. Thus, metre and second are units of length and time respectively; indeed, each defined quantity can have many units: length can be measured in metres, inches, fathoms, etc.

In the measurement of ionizing radiations and radioactivity, the International Commission on Radiation Units and Measurements, *ICRU*, is responsible for the formulation of appropriate quantities. In respect of *units*, ICRU has recommended the use of the International System, SI, which is the responsibility of the General Conference on Weights and Measures, known as *CGPM* from the name in French.

SI units are divided into three classes—base units, derived units, and supplementary units. There are seven base units, such as metre for the quantity length, kilogram for the quantity mass and second for the quantity time. Derived units are formed by combining these base units according to the algebraic relations linking the corresponding quantities, and some of these have special names, such as the watt (equal to kg m^2 s^{-3}) for the quantity power. Some of these special names are restricted to certain quantities only, as in the case of the radiation units, gray, sievert and becquerel (see Table I in the preceding paper, Conversion to SI units in radiology). The present supplementary units are radian and steradian (for plane and solid angle respectively). These three classes form a *coherent* system of units, one in which all derived units can be obtained from the base units without the introduction of numerical factors.

Let us return for a moment to the subject of quantities. In their report No. 33 (ICRU, 1980), ICRU have defined some 38 quantities relevant to the measurement of ionizing radiation and radioactivity, including a number of "rate" quantities such as absorbed dose rate. In this new report these quantities are divided into four categories. The first category, *radiometry*, deals with quantities associated with the radiation field itself, such as energy fluence. The second category, *interaction coefficients*, deals with quantities associated with the interaction of radiation and matter, such as the mass attenuation coefficient. The third category, *dosimetry*, deals with quantities that are generally products of quantities in the first and second categories, such as exposure, although they are not defined in this manner, primarily because they are usually measured directly. The fourth category is *radioactivity*.

For the present purpose, we need only consider those dosimetric quantities which are in daily use, *i.e.* those devised to provide a physical measure to correlate with actual or potential effects of irradiation. Moreover, these are the quantities which are subject to measurement for calibration purposes by Standards Laboratories, and for which the units have been endowed with special names.

UNIVERSITY COLLEGE OF MEDICINE LIBRARY

Measurement standards

Standards laboratories, such as NPL, are concerned with "measurement standards", as against "specification standards" which are the concern of organizations such as the British Standards Institution, BSI; indeed, in French there are two separate words for these respective standards, *etalon* and *norme*, to avoid any confusion between the two meanings. Measurement standards are developed to realize units of measurement of selected quantities; they are "absolute", or "fundamental", if the values are established in terms of the relevant base units without recourse to another standard of the same quantity.

Special units and SI units with special names

The principal quantities of interest in the present context are exposure, absorbed dose, dose equivalent and activity. Prior to the introduction of SI units, there were *special units* for use with these four quantities, namely, röntgen, rad, rem and curie, respectively; however, these are not coherent with SI. This means that they cannot be derived in terms of base units without the introduction of undesirable factors like 2.58×10^{-4}, 3.7×10^{10} or 0.01 (see Table I in preceding paper). It has been recommended that these special units be abandoned by 1985.

It will be appreciated that some special units do have the advantage of brevity in that reference to the unit determines the quantity also. Thus "x röntgens" can only refer to a measurement of the quantity exposure, where as "y joules per kilogram" could refer to an absorbed dose or to the calorific value of coal. However, although *special units* are on the way out, *special names* have now been given to some relevant SI units, such as the gray, sievert and becquerel. These special names may be restricted to the unit of a single quantity—like becquerel for activity, or to a limited number of quantities—like gray for absorbed dose, kerma, specific energy and absorbed dose index (these restrictions being identical to those applicable to the curie and rad respectively). Thus, in the latter instance, to avoid any ambiguity, one should specify the quantity as well as the unit, *e.g.* "an absorbed dose of x grays". Moreover one should also specify the material or medium to which the absorbed dose is given, such as to air, water or tissue. One should also note that the medium relates to the quantity, not the unit: an "absorbed dose to water" of x grays, not an absorbed dose of "x grays in water."

Some pitfalls

The adoption of special names helps to avoid misuse and errors. For example, an absorbed dose rate of "x joules per kilogram minute" is not only too long for routine use, but may be open to confusion with "x joules per kilogram per minute"; there is no problem with "x grays per minute", if the context is clear, such as in radiotherapy. On the other hand, if the context is not clear, the use of grays as the unit for both absorbed dose and dose equivalent could lead to significant errors. These two quantities can both be measured in joules per kilogram, but dose equivalent incorporates an additional (non-dimensional) weighting factor which can be as great as 20. For this reason, in the interests of safety, the CGPM agreed to the adoption of the special name sievert for the unit of the quantity dose equivalent. Similarly, the CGPM agreed to the adoption of the name becquerel as the unit of activity, to avoid potential errors in the use of prefixes with a reciprocal unit, "per second". Apart from such exceptions, the CGPM is anxious to minimize the proliferation of special names, which it deprecates.

Some problems in the choice of quantities

The introduction of SI units has led to certain problems, some of which were already present, but were brought into focus by this exercise. For example, when a therapy-level exposure meter scaled in röntgens is used to determine absorbed dose to water expressed in rads, there is rough agreement between the numerical values of the scale reading and the absorbed dose. This rough agreement no longer holds between the corresponding SI units coulomb per kilogram and gray. (Some people regard this as an asset—to demonstrate that one röntgen is *not* essentially equal to one rad!) This change has led to the alternative propositions that Standards Laboratories should either (i) abandon the measurement of exposure in favour of the quantity *air kerma*; as this can be expressed in grays, the rough numerical agreement with absorbed dose in water expressed in grays is thus restored; or (ii) calibrate instruments directly in terms of absorbed dose to water, the latter under specified conditions, as the calibration would otherwise not be unique.

Exposure, kerma and absorbed dose

Let us consider these two propositions for a few minutes. If one looks up the definitions of exposure and kerma in the ICRU Reports, it will be seen that the brief definitions given are each amplified by a series of notes; the latter are generally omitted when these definitions are quoted elsewhere, yet these notes may be directly relevant. In this instance it will be found that exposure relates to the *charges* (ions) liberated by photons in air per unit mass, whereas kerma relates to the initial kinetic *energies* liberated per unit mass; indeed, "kerma" is an acronym for Kinetic Energy Released per unit MAss. Thus exposure is (almost) the ionization equivalent of kerma in air, and the two quantities are approximately related by the factor W/e, where W is the mean energy expended per ion pair formed, and e is the electronic charge. However, one of the notes attached in the definition of exposure states that ionization resulting from the absorption of bremsstrahlung emitted by the electrons is excluded, whereas it is *not* excluded in the case of kerma. This difference, amounting to about 0.5% for 2 MV radiations, is an unwelcome factor, though of little significance at low energies, or in protection measurements. Thus, calibrations made in terms of exposure can be converted to air kerma, and these will then approximate to absorbed dose to air, provided certain conditions hold—namely "charged particle equilibrium conditions".

BCRU recommendations and CCEMRI Working Parties

Following prolonged discussions by both national and international bodies, the alternative line of calibrating instruments for photon dosimetry in terms of "absorbed dose to water, under specified conditions" has now gained more favour. The British Committee on Radiation Units and Measurements, BCRU, has prepared recommendations to this end, including the necessary reference conditions, and these have been published in The British Journal of Radiology (BCRU, 1980). Essentially the proposals are as follows. Existing exposure standards will continue to serve as the primary reference measurement, and calibrations will be expressed in coulombs per kilogram. In due course, this will be supplemented for high energy radiations by calorimetric standards, with measurements in terms of absorbed dose to carbon. In addition, derived calibration factors will be given in an addendum to the certificate which will enable the user to interpret the field instrument scale-readings directly in terms of absorbed dose to water, under specified conditions. However, these recommendations depend on the adoption by the Standards Laboratories of the relevant conversion factors for the ionization probes concerned. In order to establish agreed, and indeed improved, factors for this purpose, two working parties have now been set up by Section I (Photon and electron measurements) of the Consultative Committee on Standards for the Measurement of Ionizing Radiation, CCEMRI, of the International Committee on Weights and Measures, CIPM—which reports to CGPM. The Sections of CCEMRI provide the focus for collaboration between the world's Standards Laboratories on these topics.

Some of the advantages and limitations of the respective quantities discussed above are summarized in Table VI in the preceding paper, Conversion to SI units in radiology. This position obtained irrespective of the introduction of SI units. Finally, it will be noted that the question of the choice of the most apropriate dose equivalent quantity, expressed in sieverts, for protection measurements has not been discussed in this contribution; this topic is still subject to much debate. It is intended to provide a further Note on quantities and units in this area at a later date.

REFERENCES

Jennings, W. A., 1980. How Much Do You Know About Quantities and Units, *BIR Bulletin*, *6*, 2, 4.

British Committee on Radiation Units and Measurements, 1980. Quantities for reporting the calibration of therapy-level dosemeters in photon beams, *British Journal of Radiology*, *53*, 917.

International Commission on Radiation Units and Measurements, 1980, Radiation Quantities and Units, (ICRU Report 33) (ICRU Publications, Box 30165, Washington DC, USA).

1981, *British Journal of Radiology*, 54, 384–390

Age-related brain atrophy and mental deterioration—a study with computed tomography

By M. Ito, M.D., J. Hatazawa, M.D., H. Yamaura, M.D. and T. Matsuzawa, M.D.

Department of Radiology and Nuclear Medicine, The Research Institute for Tuberculosis, Leprosy and Cancer,
Tohoku University 4-1 Seiryo-cho, Sendai, 980 Japan

(Received August 1980 and in revised form October 1980)

Abstract

The relation of brain atrophy measured with computed tomography (CT) to mental deterioration on living people was studied. A newly improved technique for quantitative measurement of brain atrophy was developed. The pixels inside the head slices were divided into three parts; brain skull, and cerebrospinal fluid according to their CT number. The volume of brain, CSF, and cranial cavity were calculated by counting the number of pixels of each tissue.

Results from 130 normal brains showed that the CSF volume was constant at about 16 ml through 20–39 years old. After 40 years the mean CSF volume increased drastically and reached 71 ml in the seventies. The volume of the brain was standardized for comparison between different-sized heads (brain volume index: BVI). The mean BVI decreased with statistical significance after 40 years of age.

Mental function of these persons were evaluated using Hasegawa's dementia rating scale for the elderly. Progression of brain atrophy accompanied loss of mental activities ($p < 0.01$).

No organ, including the brain, escapes from senile degeneration. Senile atrophy of the brain deeply influences mental actions (Willanger *et al.*, 1968), causing one of the most important social problems. Brain atrophy in old age has been studied by pathologists (Blessed *et al.*, 1968; Morimatsu *et al.*, 1975; Tomlinson, 1977), but studies of the relation between cerebral atrophy and mental decline have been few because of the difficulties of obtaining many autopsy subjects whose mental function has been examined during their lifetime. However, CT clearly shows the gross anatomy of living brain and can offer new information about the aging of human brain. A considerable amount of research on brain atrophy using CT (Gyldensted and Kosteljanets, 1976; Huckman *et al.*, 1975; Barron *et al.*, 1976; Hahn and Rim, 1976; Robert *et al.*, 1976; Gawler *et al.*, 1976) has been reported recently, but quantitative studies are few.

In a previous communication (Yamaura *et al.*, 1980) we have shown that the brain volume determined by CT decreases drastically with advancing age. The percentage volume of the brain relative to the cranial cavity was calculated from the pixel numbers. However, the method was able to be improved slightly, allowing more accurate calculation. The improved technique for measurement of brain volume is described in the present study. Using this technique, the relation of mental deterioration to brain atrophy during aging was studied in living people and the results are reported.

Methods

The CT used was the Ohio Nuclear Delta Scanner 50 FS-2 type which has a fan-shaped X-ray beam and 24 BGO detectors. A scanning time of 25 s and a slice thickness of 8 mm was selected. The image is displayed on a 256×256 matrix, and each pixel represents tissue of $1.0 \times 1.0 \times 8.0$ mm^3 in volume. The mean X-ray attenuation value is expressed in Hounsfield units: water is 0, bone about $+1{,}000$, and air $-1{,}000$.

Head scans were performed on planes parallel to the glabellameatal basal line (GM line). The centre level of the lowermost scan was set 22 mm above the line and ten slices were obtained.

Principle of measurement

To measure the brain volume, it is necessary to know the exact attenuation value of the brain and the cerebrospinal fluid (CSF). The ventricles are usually sufficiently small for their CT numbers to be affected by partial volume phenomenon from the surrounding brain tissue. The following technique was used to minimize this artefact in obtaining the CT numbers of CSF: the outlines of the ventricles were drawn along the pixels reading 21 HU on the numerical printout of the image. This value was assumed to be the border between the brain and the CSF in our previous paper (Yamaura *et al.*, 1980). The ventricular contours on the fourth, fifth and sixth slices, counted from the GM line, were superimposed on the middle slice (Fig. 1). Among the pixels located in the region common to the ventricular contours of all three slices, those of the middle slice can be regarded as completely filled with CSF. The mean attenuation value of CSF was obtained from these pixels and was 4 HU (Table I). But this technique was useful only in subjects whose ventricles were relatively large. The attenuation of brain was also measured and was found to be 32 HU without variation with age. This was confirmed in 130 cases using the attenuation measuring programme for ROI (region of interest) (Table II).

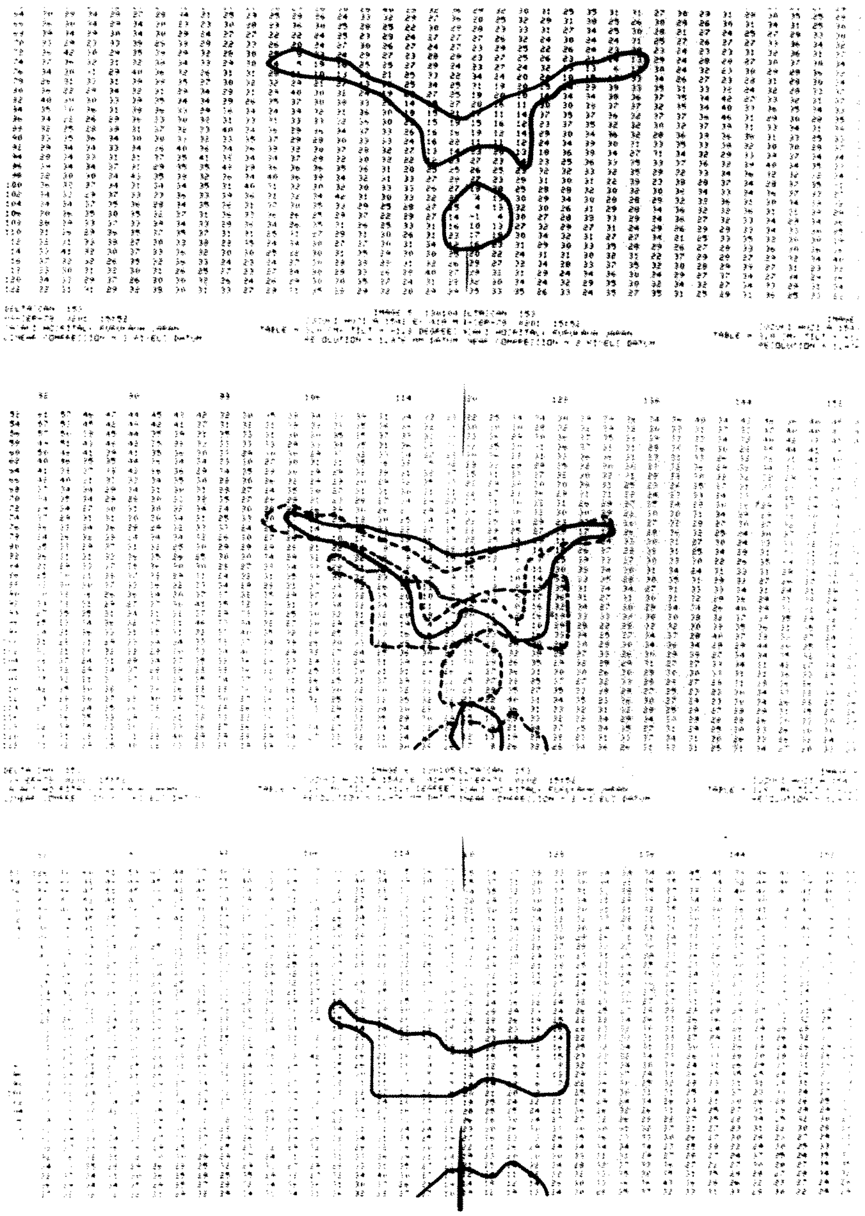


FIG. 1.

Determination of the mean CT number of the CSF. Ventricular contours are drawn on the numerical printout of the fourth, fifth and sixth slices along the pixels reading 21 HU and superimposed on the middle slice. Among the pixels common to ventricles of the successive three slices, those of the fifth slice can be regarded as completely filled with CSF and used to obtain the attenuation of CSF.

According to our basic experiments (Ito *et al.*, 1979) the border between two materials may be expressed by the average CT number of the two. Therefore the bordering CT number of ventricles should be 18 $(=(32+4)/2)$. In our previous paper (Yamaura *et al.*, 1980), the value of 21 HU was used for the border. The difference would be attributable to the overestimation of the CSF attenuation value which was much affected by the partial volume effect.

The pixels of head slices were divided into three parts using the CT numbers; bone $(\geqq 500)$, brain $(19 \leqq \text{brain} \leqq 499)$, and CSF $(\leqq 18)$. The pixels outside the cranium were excluded from the calculation by setting ROI just upon the skull (Fig. 2). Because

TABLE I

CT NUMBER OF BRAIN AND CSF

Age	n	CT no. of brain (frontal lobe) Left	Right
20–39	10	31.2 ± 1.7	32.0 ± 2.0
40–59	10	32.1 ± 2.7	31.8 ± 2.7
50–69	10	30.4 ± 1.9	31.1 ± 2.4
Total	30	31.5 ± 2.2	
Age	n	CT no. of CSF	
20–79	12	3.5 ± 1.0	

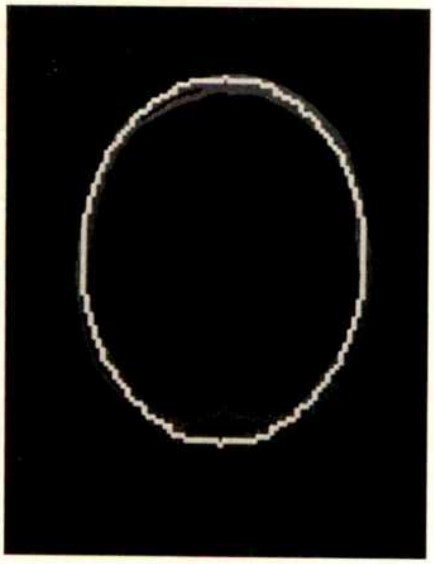


FIG. 2.

Setting of the ROI. ROI was set just upon the cranium in order to exclude the extracranial tissues. The cranial volume was obtained by subtracting the pixel number of bone (CT No. ≧ 500, grey in the figure) from the pixel number of ROI.

of unreliability of CT numbers in the region near bone, the superficial subarachnoid spaces were included with brain (Fig. 2). Volume of the suprasellar cistern, which usually appears on the first slice, was also counted as brain. From ten slices of eight mm thickness, the volume of each tissue was obtained as follows:

Volume of cranial cavity $= \Sigma$ (Total pixel number within ROI—pixel number of bone) × pixel size

Volume of CSF (Brain cavity volume, BCV) $=$ Σ (Pixel number of CSF) × pixel size

Volume of brain = Cranial volume—BCV

Pixel size $= 1.0 \times 1.0 \times 8.0$ mm^3

Each part was shown in Fig. 3.

However, the real CT number of pixels of brain and CSF overlap, partly because of the statistical fluctuation of X-ray attenuation. The degree of overlap depends upon noise and the amount of noise is affected by the quality of the X-ray tube and detectors. In order to reduce the background noise, Gaussian smoothing was carried out (Fig. 3). The major improvements in the technique compared with the previous study were the application of smoothing and more accurate determination of the mean CT number of brain and CSF as described above.

Indicator of brain atrophy

To allow for the difference in head size among individuals, the volume percentage of the brain to the cranial cavity (cranio-cerebral index: CCI) was calculated from the following equation:

$$\text{CCI} = (\text{Brain volume}/\text{cranial volume}) \times 100$$

As described in the results, the mean CCI in normal adults of 20–39 years was 98.7. This value was regarded as the standard unatrophied normal brain. The percentage of each CCI relative to this standard (brain volume index: BVI $=$ CCI/98.7 ×

TABLE II

Age	n	CT no.[1] brain	BCV (ml)[2]	CCI[2]	BVI[2]	Hasegawa's[2] Score
20–29	14	32 ± 2	16 ± 7	98.7 ± 0.6	100 ± 0.7	
30–39	20	32 ± 3	16 ± 8	98.6 ± 0.6	99.9 ± 0.6*	
40–49	29	31 ± 2	23 ± 8	98.0 ± 0.8	99.3 ± 0.9*†	25.5 ± 7.0
50–59	30	31 ± 1	38 ± 15	96.7 ± 1.2	98.0 ± 1.3†	27.5 ± 4.0
60–69	21	31 ± 1	44 ± 15	96.2 ± 1.2	97.5 ± 1.3‡	25.5 ± 5.5
70–79	16	31 ± 2	71 ± 31	93.5 ± 2.9	94.7 ± 3.0‡	21.5 ± 6.5
Total	130	31 ± 2				

[1] Mean ± SE
[2] Mean ± SD
*$p < 0.01$
†$p < 0.001$
‡$p < 0.01$

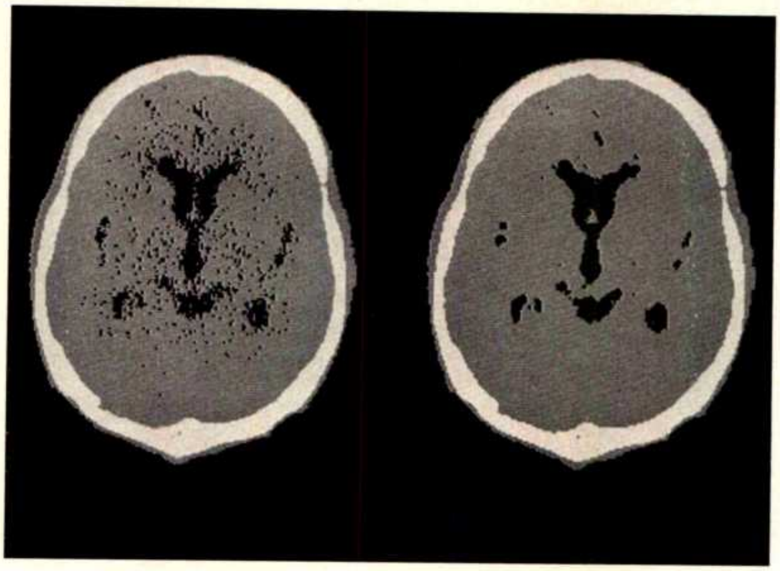


FIG. 3.
Pixels of head were divided into bone (white, CT No. ≧500), brain (grey, 19≦ CT No. ≦499), and CSF (black, CT No. ≦18). Overlapping of CT number of brain and CSF was minimized by smoothing of the image. Left, original, right, smoothed.

100) was calculated in each case as the indicator of brain atrophy.

SUBJECTS

From 1789 patients subjected to cranial CT at Sasaki Hospital, Miyagi prefecture, in northern Japan, during the period between August 1977 and June 1978, 130 normal cases (46 male and 84 female) were selected for the study. These cases were free from any brain damage due to congenital, cerebrovascular, or neoplastic diseases. Most of them were farmers.

Evaluation of mental activity

The examinees' mental activity was evaluated using Hasegawa's dementia rating scale for the elderly (Hasegawa *et al.*, 1974). The test consists of eleven questions; two testing orientation, four testing long-term memory, two testing short-term memory, two testing general knowledge and one calculating ability. This test is well-established and widely used in Japan and convenient for our purpose.

Hasegawa's dementia rating scale for the elderly is as follows:

Q1. What day is it?
Q2. Where are you now?
Q3. How old are you?
Q4. How long has passed since a recent impressive event?
Q5. Where were you born?
Q6. When did World War II finish?

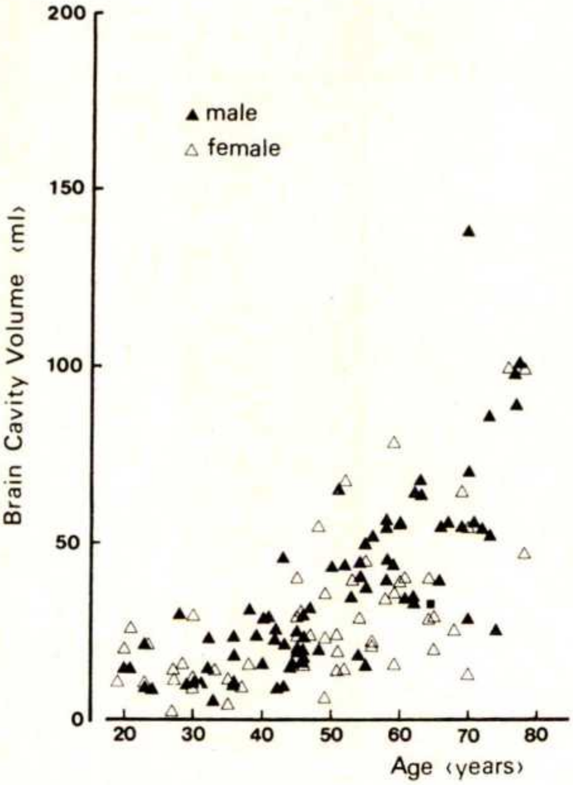


FIG. 4.
Distribution of BCV according to age and sex.

Q7. How many days are there in a year?
Q8. Who is the prime minister of Japan?
Q9. $100-7=?$ $93-7=?$ etc.
Q10. Say inversely: 6–8–2 3–5–2–9
Q11. Memory of five specimens: for example, a tooth brush, a coin, a knife, a comb, and a spoon.

RESULTS

Results are summarized in Table II. They reveal that brain atrophy advances gradually with increasing age, and brain atrophy was significantly related to mental deterioration.

Changes of BCV as a function of age of 130 cases were plotted in Fig. 4. From 20 to 39 years of age, the BCV was almost constant at 16 ml. After 40 years, the BCV gradually increased with age and reached 71 ml in the seventies (Fig. 5A). The mean CCI in the twenties was 98.7 and was used as the standard of the normal brains. The BVI of each brain was calculated from this standard. The BVI in the twenties and in the thirties were not significantly different from each other, but it decreased gradually in the forties ($BVI=99.3\pm0.9$) fifties (98.0 ± 1.3) and and seventies (94.7 ± 3.0). The decrease after the forties was significant. The standard deviation of the BVI in the seventies was evidently larger than the younger groups (Fig. 5B).

Hasegawa's score, as the measure of mental activity, had a tendency to decrease with advancing age (Table II). Though there was no statistically significant difference between age groups, the score showed a linear relation to BVI as shown in Fig. 6 ($Y=1.46X-115.5$, $\gamma=0.434$, $p<0.01$). Some representative cases are shown in Fig. 7.

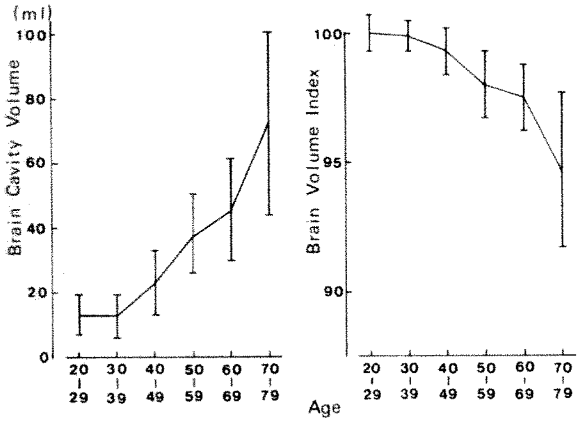
DISCUSSION

This paper may be the first report to find quantitatively a linear relation between age-related brain atrophy and mental deterioration in living persons.

The technique has been improved based on basic experiments. The mean CT number of the CSF used in the previous paper (Yamaura *et al.*, 1980) was markedly influenced by partial volume phenomenon of the surrounding tissue; this problem has been minimized. The mean CT number of the CSF and the white matter was 4 and 32 respectively. Overlapping of attenuation values of the brain and the CSF had been another problem. Reducing the background noise of images by Gaussian smoothing is necessary. As a result of these improvements, the standard deviation of the data decreased to half or less that in the previous data of BVI and a statistically significant difference was detected between patients in their thirties and forties.

Japanese pathologists have reported an age-related decrease of brain weight measured during autopsy (Fig. 8) (Minoshima, 1959). Our results in the living persons showed a similar relationship. The decrease commenced at about 40 years of age in both investigations. The agreement of the results of both studies suggests the techniques are reliable.

As the X-ray attenuation value of the brain and the CSF is influenced by neighbouring bone, the superficial subarachnoid spaces were not visualized well in the CT system. These spaces were regarded as a part of the brain. Therefore the brain cavities termed in the article consisted of the third and the lateral ventricles and deeply situated subarachnoid



A FIG. 5. B

Mean and sd of BCV (A), and BVI (B) as a function of age.

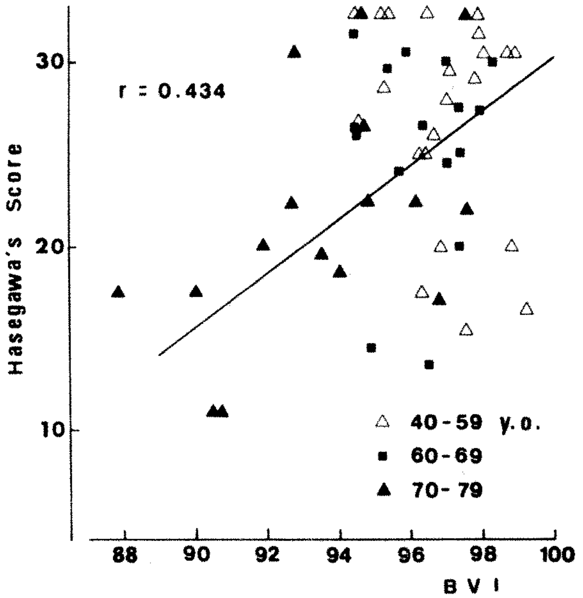
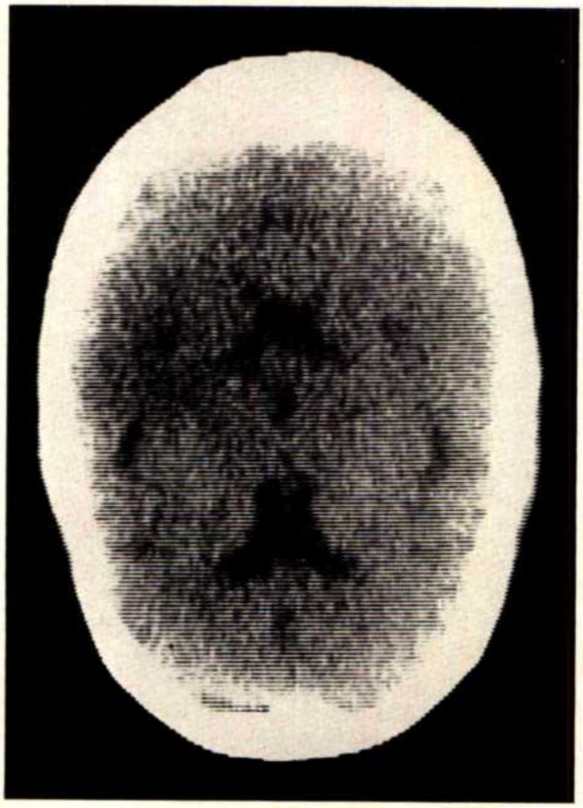
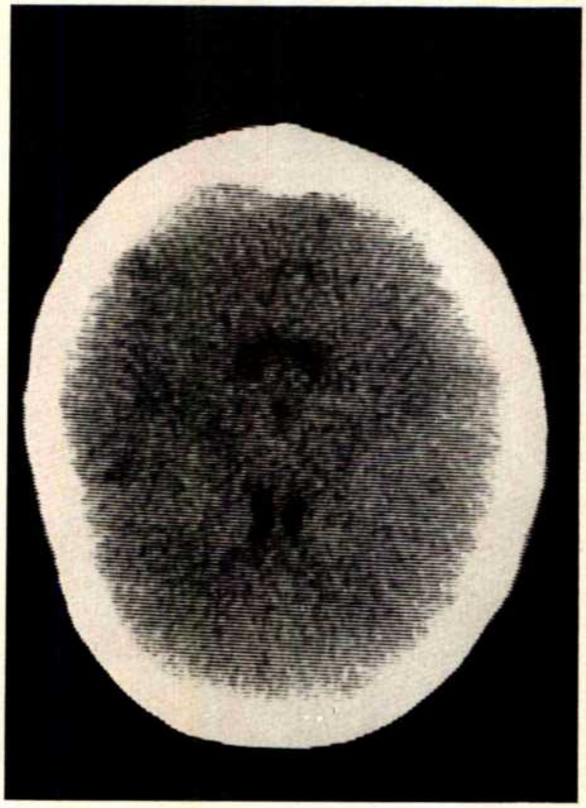


FIG. 6.

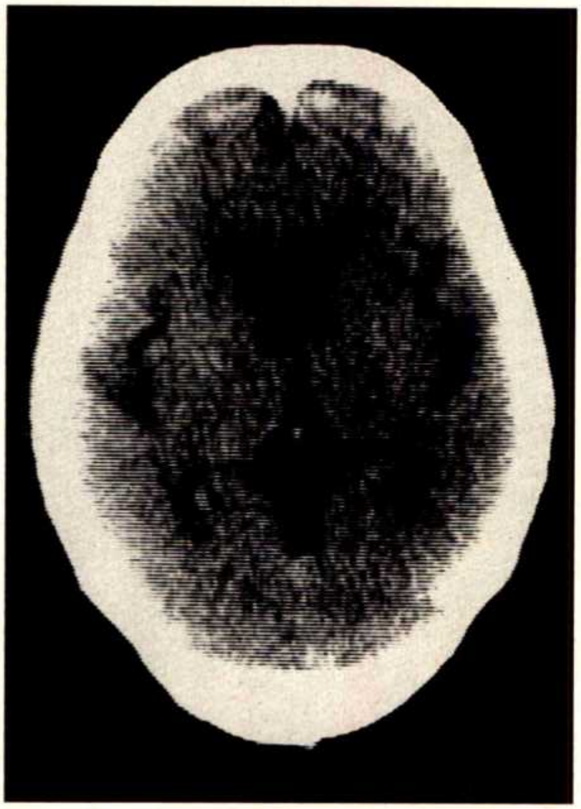
Correlation between Hasegawa's score and BVI.



A



B



C

FIG. 7.

Illustrative cases. (A) 27-year-old female. BCV = 14 ml, BVI = 100 Ventricles of this age group are usually quite small. (B) 66-year-old male. BCV = 51 ml, BVI = 97.0, Hasegawa's score = 30.5. Ventricles are larger than those of case A, but within the normal range for the sixties. (C) 70-year-old male. BCV = 71 ml, BVI = 94.6, Hasegawa's score = 19.5 According to Hasegawa's criteria, this case was classified as predementia.

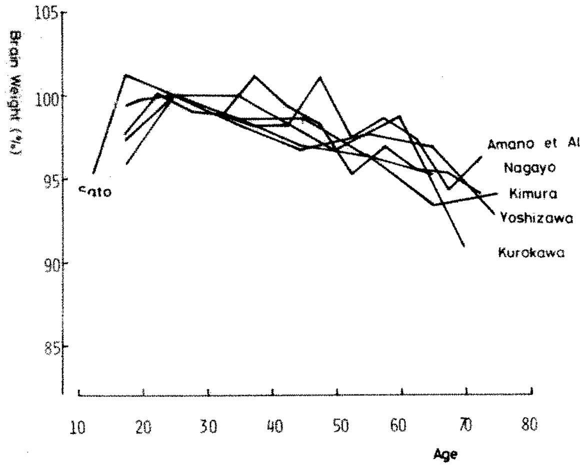


FIG. 8.

Changes of brain weight expressed as percentage of that of 20–25-year-old as a function of age (Minoshima *et al.*, 1959).

spaces; mainly the sulcus of Sylvius, the longitudinal fissure, and the superior cerebeller cistern.

Whether brain atrophy correlates with intellectual impairment is a very important problem. The aged brain presents various degenerative changes. Brody (1955) reported decrease in number of cortical cells during aging. Other degenerative changes in neurons; intracellular accumulation of lipofuscin, Alzheimer's neurofibrillary tangles, and changes in Golgi apparatus, mitochondria etc. are also observed (Brody and Vijayashankar, 1977). Probably these changes will decrease mental functions. Ventricular size evaluated by pneumoencephalography is significantly larger in demented than nondemented people (Burhenne and Davies, 1963; Engst and Lonnum, 1958; Nielsen *et al.*, 1966; Willanger *et al.*, 1968). The present study agrees with these findings.

Recently we have found that there is a close relation between brain atrophy and sclerosis of retinal arteries (Hatazawa *et al.*, 1980). It is known that arteriosclerosis is one factor related to brain atrophy (Tomlinson, 1977). Further extensive studies of this problem are necessary.

ACKNOWLEDGMENTS

We wish to express our thanks to Dr. K. Fukuda for valuable suggestions and Dr. Y. Sasaki, Dr. S. Endo and Dr. K. Yamada for supporting the study. The technical assistance of Mr. T. Sato, Mr. Y. Sugawara, Miss S. Ito and Miss N. Oyama is greatly appreciated.

REFERENCES

BARRON, S. A., JACOBS, L. and KINKEL, W. R., 1976. Changes in size of normal lateral ventricles during aging determined by computerized tomography. *Neurology, 26,* 1011–1013.

BLESSED, G., TOMLINSON, B. E. and ROTH, M., 1968. The association between quantitative measure of dementia and of senile change in the cerebral gray matter of elderly subjects. *British Journal of Psychiatry, 114,* 797–811.

BRODY, H., 1955. Organization of cerebral cortex. III. A study of aging in the human cerebral cortex. *Journal of Comparative Neurology, 102,* 511–556.

BRODY, H. and VIJAYASHANKAR, N., 1977. Anatomical changes in the nervous system. In *Handbook of the Biology of Aging.* Ed. C. E. Finch and L. Hayflick, pp. 241–261 (Van Nostrand Reinhold Company, New York, U.S.A.).

BURHENNE, H. J. and DAVIES, H., 1963. The ventricular span in cerebral pneumoencephalography. *American Journal of Roentgenology, 90,* 1176–1184.

ENGST, A. and LONUM, A., 1958. Third ventricles of 12 mm width or more. A preliminary report. *Acta Radiologica (Diagnosis), 50,* 5–11.

GAWLER, J., DU BOULAY, G. H., BULL, J. W. D. and MARSHALL, J., 1976. Computerized tomography (the EMI scanner): A comparison with ventriculography. *Journal of Neurology, Neurosurgery and Psychiatry, 39,* 203–211.

GYLDENSTED, C. and KOSTELJANETZ, M., 1976. Measurements of normal ventricular system with computer tomography of the brain. A preliminary study on 44 adults. *Neuroradiology, 10,* 205–213.

HAHN, F. J. Y. and RIM, K., 1976. Frontal ventricular dimensions on normal computed tomography. *American Journal of Roentgenology, 126,* 593–596.

HASEGAWA, K., INOUE, K. and MORIYA, K., 1974. An investigation of dementia rating scale for the elderly. (in Japanese) *Psychiatrical Medicine, 16,* 965–969.

HATAZAWA, J., ITO, M., YAMAURA, H., and MATSUZAWA, T. 1980. Brain atrophy and atherosclerosis of ocular fundus. In preparation.

HUCKMAN, M. S., FOX, J. and TOPEL, J., 1975. The validity of criteria for the evaluation of cerebral atrophy by computed tomography. *Radiology, 116,* 85–92.

ITO, M., YAMAURA, H., SATO, T., ENDO, S., YAMADA, K. OKUYAMA, S. and MATSUZAWA, T., 1979. Experimental studies on the calibration of actual organ size by computed tomography (in Japanese), *Nippon Acta Radiologica, 39,* 152–160.

MINOSHIMA, K., ed., 1959. *Nipponjin jintai seijo suchihyo.* (in Japanese), pp. 53–68. (Gihodo, Tokyo).

MORIMATSU, M., HIRAI, S., MURAMATSU, A. and YOSHIKAWA, M., 1975. Senile degenerative brain lesions and Dementia. *Journal of the American Geriatrics Society, 23,* 390–406.

NIELSEN, R., PETERSEN, O., THYGESEN, P. and WILLANGER, R., 1966. Encephalographic ventricular atrophy. *Acta Radiologica (Diagnosis), 58,* 240–256.

ROBERT, M. A., CAIRD, F. I., GROSSART, K. W. and STEVEN, J. L., 1976. Computerized tomography in the diagnosis of cerebral atrophy. *Journal of Neurology, Neurosurgery and Psychiatry, 39,* 909–915.

TOMLINSON, B. E., 1977. The pathology of dementia. In *Dementia,* Ed. C. E. Wells (F. A. Davis Company, Philadelphia). pp. 113–154.

WILLANGER, R., THYGESEN, P., NIELSEN, R. and PETERSEN, O., 1968. Intellectual impairment and cerebral atrophy. A psychological, neurological and radiological investigation. *Danish Medical Bulletin, 15,* 65–93.

YAMAURA, H., ITO, M., KUBOTA, K. and MATSUZAWA, T., 1980. Brain atrophy during aging: a quantitative study with computed tomography. *Journal of Gerontology, 35,* 492–498.

1981, *British Journal of Radiology*, *54*, 391–393

May 1981

Resolution of multiple hepatic abscesses following percutaneous transhepatic biliary drainage

By R. R. Mason, F.R.C.S., M.R.C.P., D.M.R.D.

Department of Radiology, The Middlesex Hospital, London W1N 8AA

and J. D. Irving, D.M.R.D.

Department of Radiology, Lewisham Hospital, London SE13

(*Received October 1980*)

Abstract

In two patients, multiple hepatic abscesses secondary to obstructive cholangitis have resolved following the insertion of drains into the biliary tree by the percutaneous transhepatic route, under local anaesthesia.

In the first case, the acute situation was relieved, allowing definitive management by an elective procedure rather than as an emergency. Useful short-term palliation was provided in the second case.

Percutaneous transhepatic drainage is a safe and effective alternative to emergency surgery in selected cases.

Percutaneous transhepatic cholangiography (PTC) is an established diagnostic procedure in patients with jaundice and the increased safety of the Chiba "skinny needle" technique (Tytgat, 1977) has further increased its acceptance.

The therapeutic aspects of PTC depended on the demonstration by Marions and Wiechel (1974) that a PTC catheter can be advanced into the biliary tree over a guide wire under X-ray screening control. This technique permits prolonged external drainage of the obstructed system. Furthermore, a catheter can be passed through the obstruction to provide palliative relief of jaundice by internal drainage in cases of malignant strictures of the bile ducts (Dooley *et al.*, 1979).

Resolution of multiple intrahepatic abscesses following percutaneous biliary drainage has been reported from Japan (Takada *et al.*, 1976; Nakayama *et al.*, 1978). Two further cases are described.

Case Reports

Case 1

A 46-year-old female, intolerant of fat for some years, was admitted on 2.7.79 with a ten-day history of jaundice, right hypochondrial pain, pyrexia, rigors, dark urine and pale stools. She was obese, deeply jaundiced, febrile and tender in the right hypochondrium. White cell count was 26×10^9/l. On 11.7.79 serum bilirubin was 517 mmol/l and alkaline phosphatase 36 KA units. On 16.7.79 PTC was performed. The bile duct was obstructed by a large, impacted stone (Fig. 1). Multiple tiny hepatic abscesses communicated with the biliary tree. A catheter was advanced into the biliary tree over a guide wire and the stone disimpacted. A Ring-Lunderquist catheter (with multiple side-holes) was passed through into the duodenum (Fig. 2).

Within 24 hours, the patient was apyrexial. By 24.7.79 serum bilirubin had fallen to 92 mmol/l and white cell count to 11.9×10^9/l. Cholangiography via the drainage tube (Fig. 3) showed that the biliary tree was returning to normal calibre and that the abscesses had resolved.

At laparotomy on 24.7.79 a small fibrotic gall bladder was removed together with a large stone from the common bile duct. The PTC catheter was left undisturbed for post-operative drainage and cholangiography. A T-tube was not inserted. The patient made an uneventful recovery.

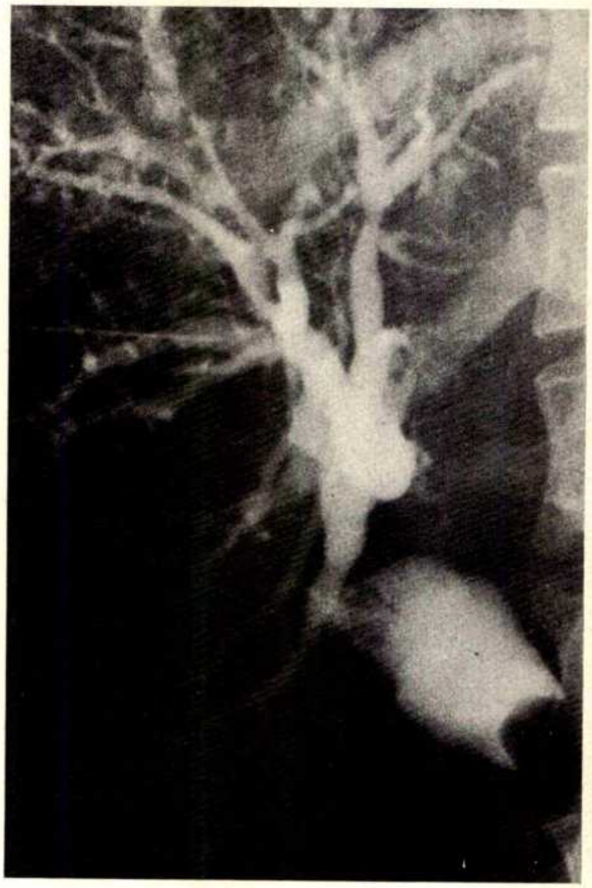


Fig. 1. *Case 1.*

PTC showing dilated biliary tree, multiple contrast-filled abscesses and complete calculous obstruction of the common hepatic duct.

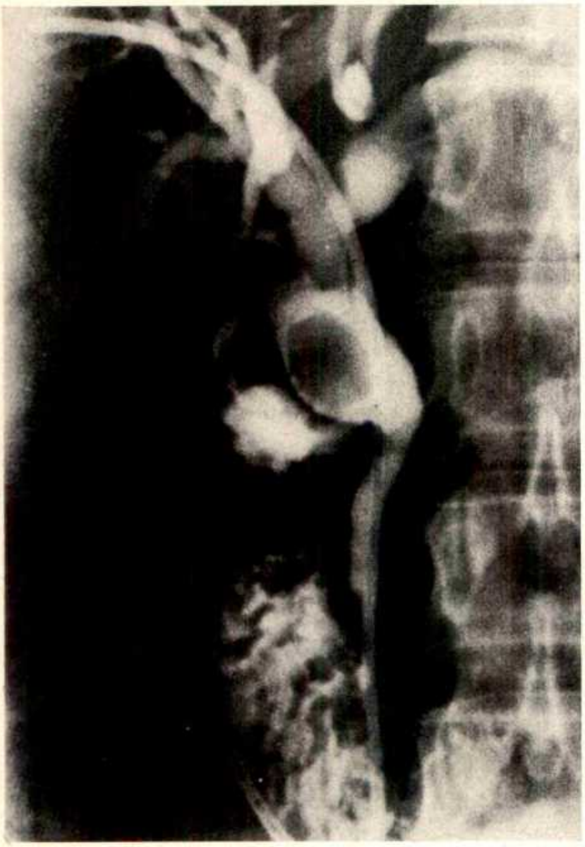


FIG. 2. *Case 1.*

A catheter has been passed alongside the stone and through into the duodenum to by-pass the obstruction.

Case 2

A 53-year-old man had a right upper lobectomy (bronchial carcinoma) in 1972, and gastrectomy (gastric carcinoma) in February 1978. The gastrectomy was complicated by a sinus which drained pus for over a year and was shown by sinography to communicate with a cavity below the liver. In March 1979, laparotomy was performed for jaundice. The findings were a dilated gall bladder and a large, hard mass surrounding the extrahepatic bile ducts. Cholecyst-jejunostomy was performed. Histological examination of a biopsy specimen failed to reveal tumour.

The jaundice abated after the by-pass operation, but over the ensuing months two brief attacks of cholangitis occurred. He was transferred during a third severe attack of cholangitis, having been pyrexial and deeply jaundiced for three weeks. On admission, he had a fever of 39.5°C and a white cell count of 47×10^9/l. His condition was considered surgically irremediable.

Two drains were inserted into the biliary tree under local anaesthesia by the percutaneous transhepatic approach. The ducts were dilated down to the level of a complete obstruction in the common hepatic duct. Countless abscesses were shown, communicating with the biliary tree (Fig. 4). Sixty millilitres of pus drained immediately and the patient became apyrexial within an hour. The catheters were left for permanent drainage.

Cholangiography three days later showed that the abscesses had resolved and that the biliary tree was returning to its normal calibre (Fig. 5).

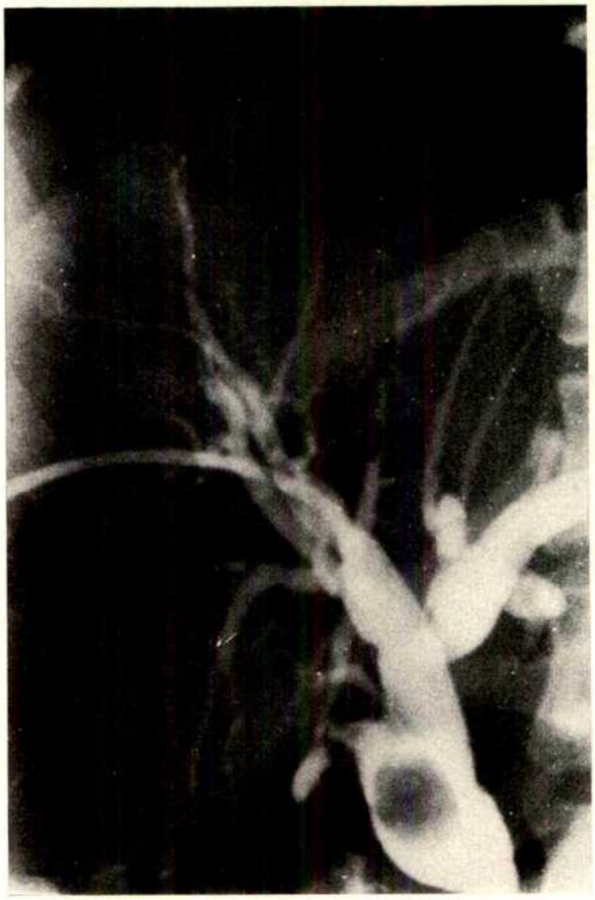


FIG. 3. *Case 1.*

Cholangiogram performed eight days after drainage. The abscesses have resolved and the biliary tree is only minimally dilated.

The jaundice improved temporarily. He died six weeks later. Post-mortem examination revealed extensive tumour recurrence within the abdomen.

DISCUSSION

Multiple hepatic abscesses are usually secondary to extrahepatic biliary obstruction and cholangitis. Patients with this condition are jaundiced and febrile and may have bacteraemia. They are poor operative risks. PTC confirms the diagnosis of abscesses and shows the site, and usually the cause, of the obstruction. The introduction of a catheter at the time of PTC allows drainage, either to improve the patient's condition prior to surgery, or as a definitive management.

Duodenoscopic sphincterotomy (Cotton, 1980) provides an alternative emergency technique in patients whose acute cholangitis is secondary to duct stones. However, therapeutic PTC is simpler, and requires no expensive equipment.

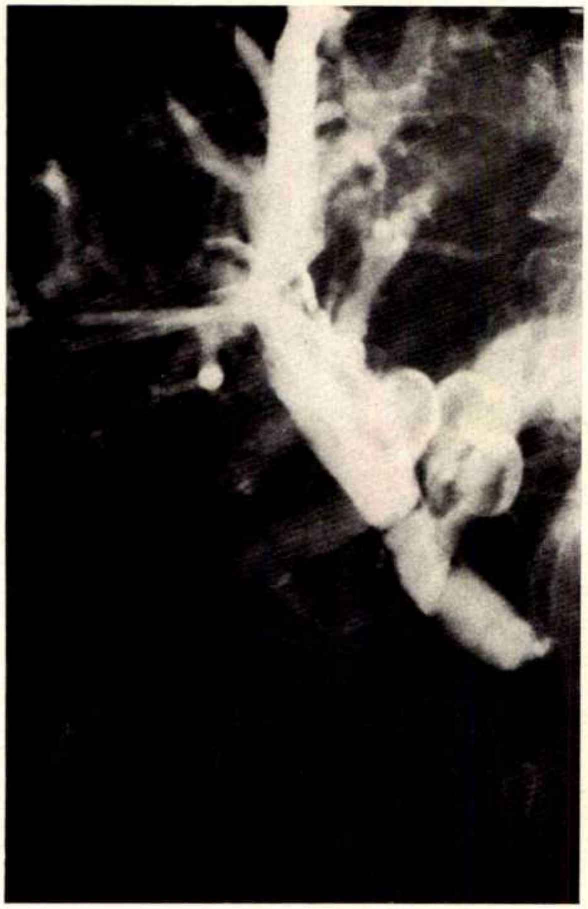


FIG. 4. *Case 2.*
PTC showing dilated biliary tree, multiple abscesses and complete obstruction of the common hepatic duct.

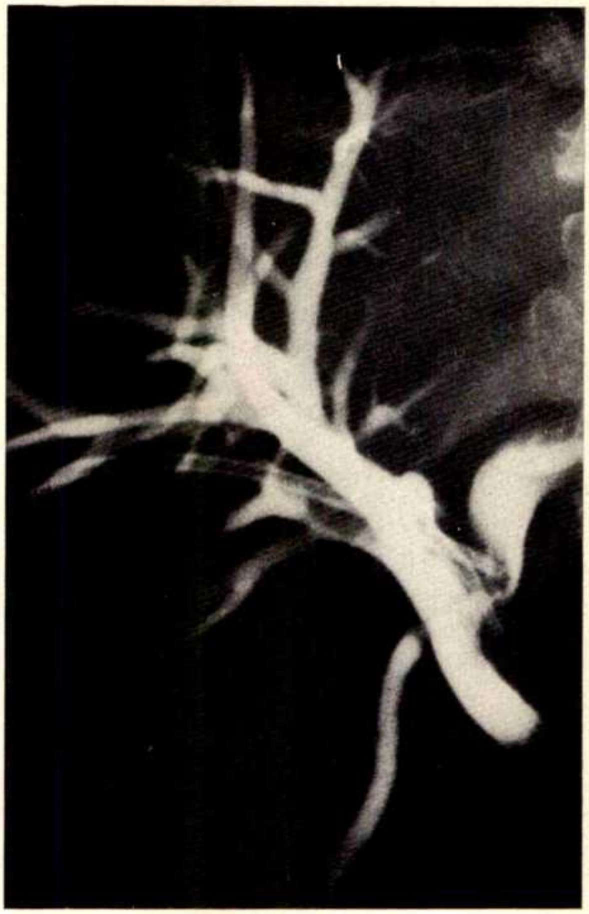


FIG. 5. *Case 2.*
Cholangiogram three days later. The abscesses have resolved and the ducts are less dilated.

Surgical emergency decompression of the bile duct is stated to be mandatory in acute suppurative obstructive cholangitis, even in the apparently moribund (Sherlock, 1975). Emergency decompression by the less traumatic procedure of percutaneous transhepatic drainage may be a preferable alternative.

ACKNOWLEDGMENTS

The cases were reported by kind permission of Dr. P. B. Cotton and Mr. H. I. LeBrun.

REFERENCES

COTTON, P. B., 1980. Non-operative removal of bile duct stones by duodenoscopic sphincterotomy. *British Journal of Surgery*, *67*, 1–5.

DOOLEY, J. S., DICK, R., OLNEY, J. and SHERLOCK, S., 1979. Non-surgical treatment of biliary obstruction. *Lancet*, *ii*, 1040–1043.

MARIONS, O. and WIECHEL, K-L., 1974. *Opuscula Medica Suppl. 32*, p. 1050.

NAKAYAMA, T., IKEDA, A. and OKUDA, K., 1978. Percutaneous transheptic drainage of the biliary tract. *Gastroenterology*, *74*, 554–559.

SHERLOCK, S., 1975. *Diseases of the Liver and Biliary System.* 5th ed. (Blackwell Scientific Publications, Oxford), p.751.

TAKADA, T., HANYU, F., KOBAYASHI, S. and UCHIDA, Y., 1976. Percutaneous transhepatic cholangial drainage: direct approach under fluoroscopic control. *Journal of Surgical Oncology*, *8*, 83–97.

TYTGAT, G., 1977. Percutaneous transhepatic cholangiography. *Scandinavian Journal of Gastroenterology*, *12*, suppl. 47, p. 27.

1981, *British Journal of Radiology*, *54*, 394–397

Ultrasound guided percutaneous abdominal abscess drainage

By D. P. MacErlean, F.R.C.R., A. P. Owens, F.F.R.R.C.S.I. and J. B. Hourihane, F.R.C.R.

Department of Diagnostic Radiology, St. Vincent's Hospital, Dublin 4, Ireland

(*Received October 1980*)

ABSTRACT

Traditional management of abdominal abscess is according to classical surgical methods. Catheter or needle drainage of these abscesses, using ultrasound both as an imaging modality and as a monitor of technique, offers a safe and rapid method of drainage of all types of abdominal abscess and eliminates surgery in many patients. Eleven abdominal and retroperitoneal abscesses were satisfactorily drained under ultrasound control in ten patients. No abscess recurred, but in three patients subsequent surgery was performed, in one because the abscess was multiloculated, and in the other two to exclude underlying malignancy.

Intraperitoneal and retroperitoneal abscesses are traditionally drained surgically according to standard approaches (Altemeier *et al.*, 1973; Ariel and Kazarian, 1971). Postoperative subphrenic abscesses thus treated carry mortality rates of between 7.5% and 43% and recurrence rates of up to 49% (DeCosse and Fox, 1974).

Transabdominal biopsy techniques (Holm *et al.*, 1975) show that fine needle puncture through the peritoneal cavity causes no appreciable morbidity and that, apart from cytological diagnoses, fluid-containing masses may be successfully aspirated (Haaga *et al.*, 1977; Ennis and MacErlean, 1980; Smith and Bartrum, 1974; Gronvall *et al.*, 1977; MacErlean *et al.*, 1980).

Ultrasonic localization of intra-abdominal abscess is well documented (Doust *et al.*, 1977; Laing and Jacobs, 1977). Confirmation of the presence of pus using aspiration has been reported (Smith and Bartrum, 1974), but simultaneous therapeutic aspiration has been attempted in only a few instances (Gronvall *et al.*, 1977). Gerzof *et al.* (1979) have reported aspiration of abdominal abscesses using both ultrasonic and CT localization.

Our experience of therapeutic aspiration of 11 abscesses under ultrasound control alone is presented.

METHOD

Each abscess was localized using a commercially available grey scale ultrasound machine with a 3.5 MHz transducer. Size and site of the abscess were estimated along with optimum approach and angle. A 16 gauge needle with outer Teflon sheath was advanced during suspended respiration to the distal abscess cavity wall, usually through a biopsy transducer.

When the cavity was of small volume, or continuous drainage undesirable, *e.g.* abscess lying directly behind bowel, the entire contents were aspirated immediately. Saline was then introduced and the cavity irrigated until the returning fluid was clear. Antibiotics were then directly introduced into the cavity, the sheath withdrawn, and follow-up sonography performed.

When the abscess cavity was of large volume and continuous drainage desirable, a J guide wire was introduced through the sheath, and then a size 8F pigtail catheter advanced over the wire. The introduction of saline and antibiotics were the same as for direct aspiration. The catheter was then sutured directly to the skin and left *in situ* until free drainage stopped.

RESULTS (TABLE I)

Surgical drainage following percutaneous drainage was required in three patients. Two of these had intrahepatic abscesses, one of which was multilocular and in which it was believed that adequate drainage had not been achieved using percutaneous drainage alone. Surgery in the other two patients was performed to trace the abscess source and to rule out underlying neoplasia.

Percutaneous techniques sufficed in management of the remaining patients. A single needle aspiration was adequate in three patients. Four patients (five abscesses in all) needed continuous catheter drainage for periods varying from four to 25 (mean 9.8) days. No abscess recurrence was noted. No complications were observed in any patient.

ILLUSTRATIVE CASE REPORT

A 67-year-old female (patient No. 9), presented with a three-day history of fever, and had pain and tenderness in the right subcostal region. There was a leucocytosis and elevated sedimentation rate. There was no history of previous upper gastrointestinal complaints.

A barium meal showed leakage of contrast from a deformed duodenal cap into a large gas-containing subphrenic abscess (Fig. 1). Sonography confirmed the presence of a large transonic mass in the right anterior subphrenic space, extending into the subhepatic area (Fig. 2).

A size 8F pigtail catheter was inserted in the midclavicular line and advanced over the dome of the right hepatic lobe. A large amount of gas escaped, following which 700 ml of pus were aspirated, and drainage was continued over a period of ten days during which a further 900 ml of pus drained (Fig. 3). At the initial procedure, 1 g of an ampicillin/cloxacillin compound was instilled, and while pus continued

TABLE I

PERCUTANEOUS ABSCESS DRAINAGE

Patient number	Age	Sex	Abscess site	Previous surgery	Pus volume organism (if known)	Mode of aspiration	Drainage route	Follow up period (months)	Recurrence	Subsequent surgery
1	69	F	Intrahepatic	No	150 ml	Needle	Trans-peritoneal	15	No	Drainage of loculated Abscesses
2	45	M	Intrahepatic	No	400 ml Bacteroides	Catheter	Trans-peritoneal	9	No	Laparotomy ?underlying neoplasia
3	50	M	Retro-peritoneal	No	150 ml Streptococcus faecalis	Catheter	Extra-peritoneal	Died 1 day post-op. myocardial infarction	—	Laparotomy ?underlying neoplasia
4	27	M	Retro-peritoneal	No	30 ml Staphylococcus aureus	Needle	Extra-peritoneal	8	No	No
5	42	M	Retro-peritoneal	No	400 ml Staphylococcus aureus	Catheter	Extra-peritoneal	9	No	No
6	22	F	Intrarenal	No	100 ml	Needle	Extra-peritoneal	24	No	No
7	28	F	Pelvic	Hysterectomy	150 ml Streptococcus faecalis	Needle	Trans-peritoneal	8	No	No
8	60	M	Subphrenic	Vagotomy and pyloroplasty	500 ml	Catheter	Trans-peritoneal	12	No	No
9	67	F	Subphrenic	No	700 ml Coliforms	Catheter	Trans-peritoneal	9	No	No
10	52	M	(A) Subphrenic	Laparotomy (division of adhesions)	600 ml	Catheter	Trans-peritoneal	3	No	No
			(B) Rectus sheath		120 ml	Catheter	Extra-peritoneal	3	No	No

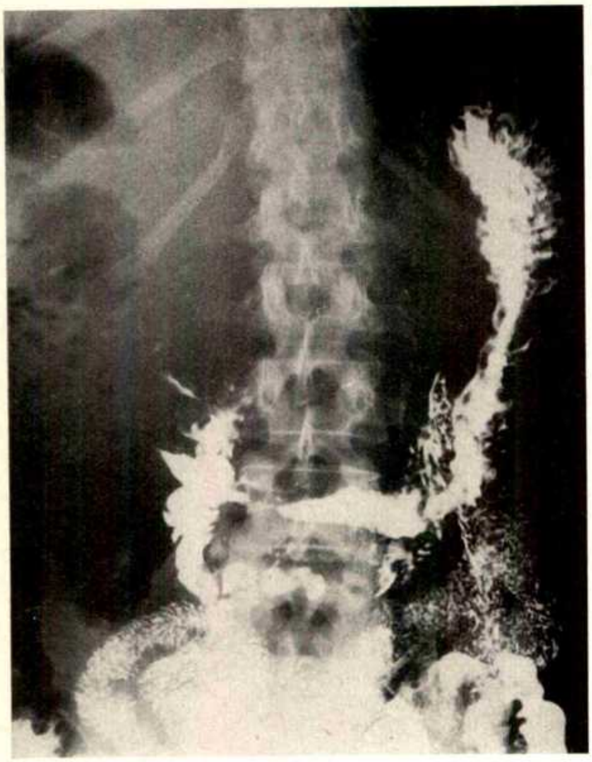


FIG. 1.
Upper GI series. Barium is seen tracking from the deformed duodenal cap into a large subphrenic abscess.

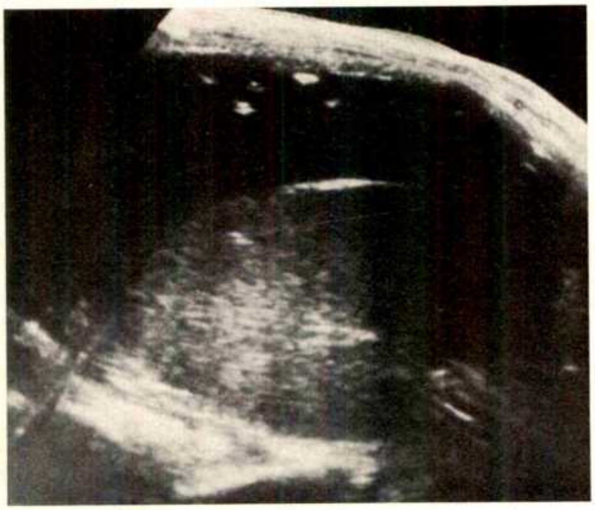


FIG. 2.
Decubitus sonogram of right upper quadrant. A large transonic mass (abscess) is seen between the abdominal wall and liver. Echoes within the mass represent gas in the abscess.

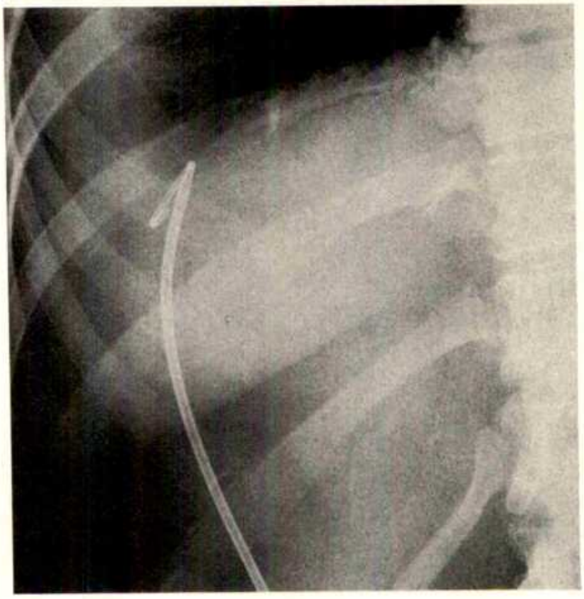


FIG. 3.
Post-drainage, catheter *in situ*. Right basal effusion present.

to drain the patient was maintained on intravenous feeding. The catheter was removed at ten days because sonography showed that pus accumulation had ceased and because the patient was then apyrexial. Oral feeding was then started, surgery avoided, and no complications were noted.

The patient remains well nine months later.

DISCUSSION

Percutaneous drainage of abdominal abscesses, either intra or extraperitoneal, is a simple procedure when accurate localization of the lesion is obtained ultrasonically.

There appears to be little danger in transfixing organs such as small bowel in order to gain access to an abscess, although previous workers mention this as a particular hazard (Gerzof *et al.*, 1979). Blood cultures where estimated in our patients have remained negative during the period of the procedure and afterwards. A possible hazard of causing direct extension of the abscess, due to poor technique, remains. However, we feel this risk to be low provided the operator is experienced in both catheter techniques and ultrasonography.

The benefits of the procedure are many, and contrast with the low morbidity observed.

The procedure may be performed on a very ill patient who is unfit for surgery. Alternatively, it may be used as an interim measure while surgery is being considered, but surgery in fact may be avoided altogether in a high proportion. Patients tolerate the procedure well, as only local anaesthetic is required, and if necessary the procedure can be repeated. A particular group of patients who may expect to benefit are those with post-operative abscesses, who are often extremely ill and in whom a high operative mortality may be expected (DeCosse and Fox, 1974). Ensuing benefits include a shorter hospital stay.

Although computerized tomography has been shown to be a highly accurate method of demonstrating abdominal abscesses (Haaga *et al.*, 1977; Halber *et al.*, 1979), ultrasound is cheaper, does not involve ionizing radiation, allows detailed repeat examination of a particular area of the abdomen followed by "on the spot" drainage procedure and continuing imaging as necessary. In conclusion we feel that the development of percutaneous abscess aspiration offers an effective and safe new procedure in the growing field of interventional radiology, and that ultrasound alone will usually provide sufficient information to establish diagnosis and guide therapy.

REFERENCES

Altemeier, W. C., Culbertson, W. R., Fullen, W. D. and Shook, C. D., 1973. Intra-abdominal abscesses. *American Journal of Surgery, 125*, 70–79.

Ariel, I. M. and Kazarian, K. K., 1971. *Diagnosis and treatment of abdominal abscesses* (Williams and Wilkins, Baltimore), p. 87.

DeCosse, J. J. and Fox, P. S., 1974. Subphrenic abscess. *Surgery Gynecology and Obstetrics, 138*, 841–846.

Doust, B. D., Quiroz, F. and Stewart, J. M., 1977. Ultrasonic distinction of abscesses from other intraabdominal fluid collections. *Radiology, 125*, 213–218.

Ennis, M. G. and MacErlean, D. P., 1980. Percutaneous aspiration biopsy of abdomen and retroperitoneum. *Clinical Radiology, 31, 611-616.*

Gerzof, S. G., Robbins, A. H., Birkett, D. H., Johnson, W. C., Pugatch, R. D. and Vincent, M. E., 1979. Percutaneous catheter drainage of abdominal abscesses guided by ultrasound and computed tomography. *American Journal of Roentgenology, 133*, 1–8.

Gronvall, J., Gronvall, S. and Hegedus, V., 1977. Ultrasound guided drainage of fluid containing masses using angiographic catheterization techniques. *American Journal of Roentgenology, 129*, 997–1002.

Haaga, J. R., Alfidi, R. J., Havrilla, T. R., Copperman, A. M., Seidelmann, F. E., Reich, M. E., Weinstein, A. J. and Meaney, T. F., 1977. CT detection and aspiration of abdominal abscess. *American Journal of Roentgenology*, 128, 465–474.

Halber, M. D., Daffner, R. H., Morgan, C. L., Trought, W. S., Thompson, W. M., Rice, R. P. and Korobkin, M., 1979. Intraabdominal abscess; current concepts in radiologic evaluation. *American Journal of Roentgenology, 133*, 9–13.

Holm, H. H., Pedersen, J. F., Kristensen, J. K., Rasmussen, S. N., Hancke, S. and Jensen, F., 1975. Ultrasonically guided percutaneous puncture. *Radiologic Clinics of North America, 13*, 493–503.

Laing, F. C. and Jacobs, R. P., 1977. Value of ultrasonography in the detection of retroperitoneal inflammatory masses. *Radiology, 123*, 169–172.

MacErlean, D. P., Bryan, P. J. and Murphy, J. J., 1980. Pancreatic pseudocyst: management by ultrasonically guided aspiration. *Gastrointestinal Radiology, 5*, 255–257.

Smith, E. H., and Bartrum R. J., Jr, 1974. Ultrasonically guided percutaneous aspiration of abscesses. *American Journal of Roentgenology, 122*, 308–312.

Book review

Alimentary Tract Radiology. Vol. 3. Ed. A. R. Margulis and H. J. Burhenne. 1979. pp. xii+689. (YB Medical Publishers, Chicago/London). £54
ISBN 0-8016-3134-3

Those familiar with Volumes 1 and 2 of this series *Alimentary Tract Roentgenology* have looked forward to the publication of the third volume. They will also note the subtle title change from *Alimentary Tract Roentgenology* to *Alimentary Tract Radiology* which results from the increased influence of the newer imaging methods in the investigation of abdominal disease. Thus the third volume under the editorship of Burhenne and Margulis is confined to the newer modalities of ultra-sound and CT scanning together with nuclear medicine.

To cover these wide and rapidly changing subjects the editors have assembled as contributors many of the international experts in their field. Whilst this has undoubtedly enabled the rapid production of a book of considerable size, it has also led to occasional repetition and variation in style.

The volume is divided into sections; the initial section is devoted to the technical aspects and anatomy of each modality which may be particularly useful to radiologists who have only a very limited knowledge of the physical basis of these techniques. An attempt is also made to indicate possible future ways in which advances may occur.

Each subsequent section describes the imaging of particular abdominal organs by each technique. A valuable concluding chapter is included in each section in which the relative merits of each modality are discussed by an impartial author. Although a somewhat unusual inclusion in such a text, a clear understanding of the relative merits of each modality becomes daily more relevant to both qualified and in-training radiologists. This aspect is equally relevant to clinicians involved in abdominal disease who, faced with an increasing number of imaging approaches to the same problem, do not always request the most appropriate.

The text is generally well written, objective and for the most part very well illustrated. Many ultrasonographers in this country in particular will be pleased to note the high incidence of white on black images not normally found in American publications.

Whilst this large and excellent book may prove too expensive to be purchased by trainee radiologists, it should certainly be included in any suggested reading list and would be an invaluable addition to the departmental library; perhaps not only the library of the Department of Radiology but also the Departments of Surgery and Medicine.

D. M. King.

1981, *British Journal of Radiology*, *54*, 398–402

Modification of gallium-67 citrate distribution in man following the administration of iron

By F. W. Smith, M.B., Ch.B., D.M.R.D., F.F.R.

Department of Nuclear Medicine, Aberdeen Royal Infirmary, Foresterhill

and P. P. Dendy, Ph.D.

Department of Bio-Medical Physics and Bio-Engineering, University of Aberdeen, Foresterhill, Aberdeen AB9 2ZD

(Received September 1980 and in revised form December 1980)

ABSTRACT

Current imaging techniques with ^{67}Ga citrate for the localization of malignant or inflammatory lesions have a number of major limitations. In an effort to improve the lesion-to-background ratio and to reduce the time between ^{67}Ga citrate injection and performing the scan, the ^{67}Ga citrate injection is now routinely preceded by injection of iron-sorbitol citric acid (Jectofer).

A series of 147 patients has been studied and shows that (a) the diagnosis can be made at 24 h in 80% of the cases, and (b) when 24 h and 48 h images are read together, diagnosis is at least as accurate as by the standard method, which requires a 72 h interval between injection and scanning. The major differences in appearance are lower activity in the soft-tissue background, relative absence of colonic activity at 24 h and visualization of the bladder in about 40% of cases.

We believe that by saturating the free transferrin with iron, uptake into soft tissues and bone is sufficiently modified to enhance the lesion-to-background ratio, thereby making earlier imaging and diagnosis possible.

One of the major limitations to the use of ^{67}Ga citrate for localization of malignant tumours, notably lymphoma, and inflammatory lesions is the presence of high activity in the normal soft tissues. If images are made 24 h after the injection of ^{67}Ga, they are confused by the high normal soft-tissue and blood-pool activity. The standard procedure is to scan at 72 h, when interpretation above the diaphragm can be made with reasonable confidence, but decisions about the abdomen and pelvis may be difficult due to the activity of excreted ^{67}Ga within the colon. Further disadvantages of imaging at 72 h after injection are the delay in issuing a report and the fact that a higher activity has to be administered to allow for decay of ^{67}Ga.

The mechanisms of ^{67}Ga transport and metabolism are still not fully understood. When ^{67}Ga citrate is injected intravenously, most of it binds loosely to plasma proteins, especially transferrin and lactoferrin (Hoffer, 1978). In many respects ^{67}Ga acts as an iron analogue and factors which influence the uptake of ^{59}Fe by tumour cells have a similar effect on the uptake of ^{67}Ga (Terner *et al.*, 1979). Sephton and De Abrew (1979) have shown in mice that although the presence of excess iron at the time of injection causes some reduction in tumour uptake of ^{67}Ga, it has a much greater effect on reducing the soft-tissue uptake, thus suggesting that the visualization of abnormal uptakes may be improved.

As most of the work on ^{67}Ga transport and metabolism has been performed in either animal models or cell culture, we felt that no further improvement of the ^{67}Ga scan as a diagnostic test could be made until the effects of iron on the distribution of ^{67}Ga in humans had been assessed. We therefore conducted a preliminary study with 30 patients, inducing hyperferraemia two hours before injection. All patients given Jectofer showed a considerable increase in plasma iron concentration and in iron saturation, 19 of them showing over 95% saturation. This demonstrated that, by saturating the free transferrin with iron before injection of ^{67}Ga, uptake into normal soft tissues was modified sufficiently to enhance the lesion-to-background ratio, thereby making earlier imaging possible (Smith *et al.*, 1980). Results on a small group of patients rendered hyperferraemic *after* injection of ^{67}Ga citrate have recently been reported to Sephton and Martin (1980).

This paper presents clinical data on a much larger group of patients investigated by our method of inducing hyperferraemia before injection of ^{67}Ga citrate.

MATERIALS AND METHOD

One hundred and forty seven patients referred for gallium scan, either for the staging of lymphoma or the investigation of undiagnosed pyrexia, were studied. Only patients taking oral iron preparations were excluded. Each patient received 100 mg Jectofer intramuscularly two hours before an intravenous injection of ^{67}Ga citrate 55 MBq (1.5mCi). No side effects attributable to the iron were suffered by any of the patients. Each patient was imaged with an El Scint dual-headed whole-body scanner, using VC 3 collimators and a broad energy window centred on 195 keV, 24 h after the injection of ^{67}Ga. If at 24 h

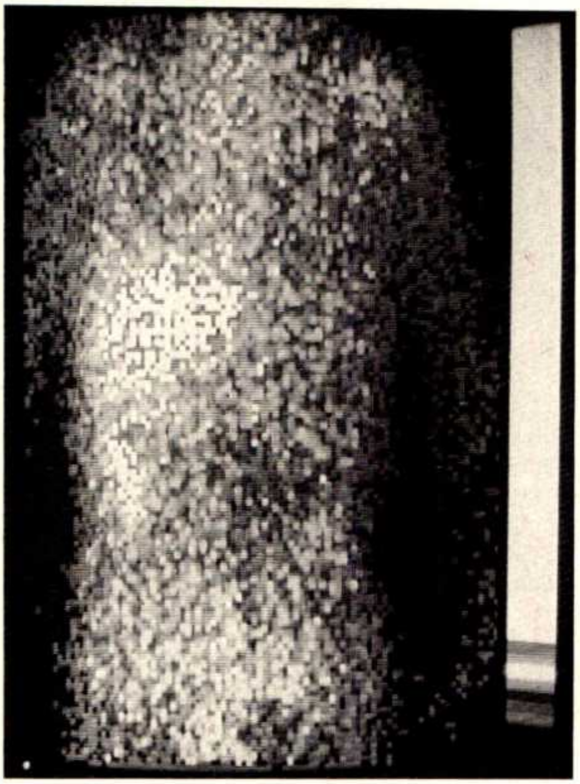


FIG. 1.

Anterior view at 24 h of the normal distribution of ^{67}Ga activity in a patient who had not been treated with Jectofer. The high soft-tissue activity obscures the chest and abdomen.

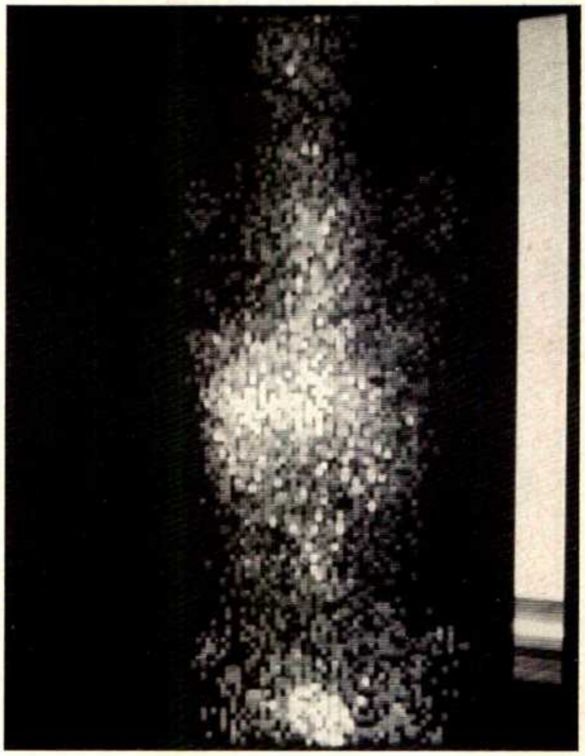


FIG. 2.

Anterior view at 24 h of the normal distribution of ^{67}Ga in a patient who had been pretreated with Jectofer. There is marked uptake in the skeleton with a low soft-tissue background. The chest and abdomen are clear and no colonic activity is seen, but activity is present in the bladder.

the mediastinum appeared widened or if there was a significantly high accumulation of ^{67}Ga in the colon, the scan was repeated at 48 h following a washout enema. All scans were read by two observers and clinical follow-up was made comparing the results of the scan with the clinical findings, chest radiographs, mediastinal tomography, lymphangiography, node biopsy and exploratory laparotomy where applicable.

In addition, urine was collected from 15 patients and the amount of ^{67}Ga excreted in the first 24 h after injection was measured using a Nuclear Enterprises Gamma-well counter. After background correction, the total activity in the urine was calculated, corrected for decay and expressed as a percentage of the administered activity.

RESULTS

Typical normal scan appearances at 24 h in the absence and presence of Jectofer are shown in Figs. 1 and 2 respectively.

Of the 147 patients studied, 58 were suffering from non-Hodgkin's lymphoma, 36 from Hodgkin's lymphoma and the remaining 53 were investigated for a wide variety of inflammatory conditions. When the scans were read at 24 h after injection, the overall diagnostic accuracy was high, the correct diagnosis and extent of disease being demonstrated in 118 cases (80%). Over-estimation of the extent of disease (overdiagnosis) occurred in 25 cases (17%) and underestimation (underdiagnosis) of the extent of disease was made in eight cases (5%) (Table I).

These observations compare favourably with previous experience of diagnostic accuracy in this hospital; in a series of 138 patients not given Jectofer and scanned at 72 h, the gallium scan was shown to agree with chest radiographic appearances in 70% of cases. In the abdomen, taking the gallium scan appearances of the para-aortic and iliac nodes together, there was agreement in 65% of cases when compared with lymphography and 74% when compared with the laparotomy findings (King *et al.*, 1981).

TABLE I

All cases

	Patients	Correct diagnosis	Overdiagnosis	Underdiagnosis
Total	147	118 (82%)	25 (17%)	8 (5%)
Non-Hodgkins' lymphoma	58	42 (73%)	13 (22%)	5 (8.5%)
Hodgkins' lymphoma	36	27 (75%)	8 (22%)	2 (5.5%)
Other	53	49 (92%)	4 (7.5%)	1 (2%)

Note that in most of the rows in both Tables I and II there is a small number of patients who were overdiagnosed in one part of the body and underdiagnosed in another; hence the apparent discrepancy in some additions.

TABLE II

Cases of pyrexia of unknown origin

	Patients	Correct diagnosis	Overdiagnosis	Underdiagnosis
Total	53	49 (92%)	4 (7.5%)	1 (2%)
Positive	33 (62%)	28 (85%)	4 (12%)	1 (3%)
Negative	20 (38%)	20 (100%)	0	0

Positive: Those with localized inflammatory lesions or malignancy.
Negative: Those with no localized lesion in which ^{67}Ga uptake would be anticipated.

Returning to Table I, when the three groups are examined separately the results are very similar for the two lymphoma groups, the correct diagnostic rate being about 73% and the rate of overdiagnosis about 22%. The group of patients investigated for other conditions showed a much higher rate of correct diagnosis (92%) and a very low false-positive overdiagnosis rate of 7.5%. This was probably due in part to the high number of normal scans in this group. Of the 53 patients investigated for undiagnosed pyrexia, 20 (38%) had normal scans (Table II). In none of these cases was evidence of malignancy or localized inflammatory lesion demonstrated by any other means to account for their pyrexia.

Analysis of the 25 false-positive results indicated that in 17 cases (68%) overdiagnosis was due to the presence of a widened, active mediastinum. When these patients were rescanned at 48 h, only five of them appeared abnormally active. Figure 3 demonstrates a patient in whom the mediastinum appears abnormal at 24 h and normal at 48 h. The eight remaining patients (32%) were overdiagnosed because of localized collection of ^{67}Ga in the abdomen, subsequently shown to have been in the large bowel. Six of the abnormal collections were in the caecum and two in the transverse colon.

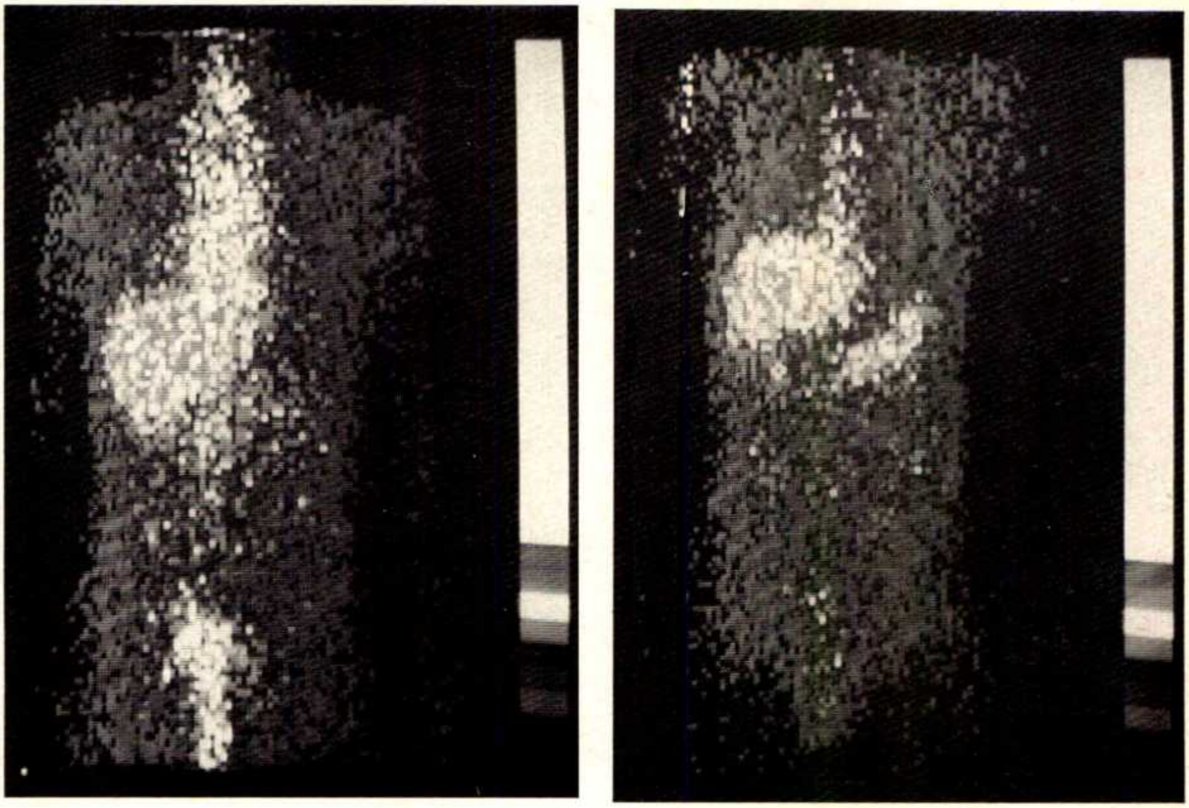
Review of the results combining the 118 correct diagnoses at 24 h with the results of the 25 patients rescanned at 48 h gives a total of 138 (94%) correct diagnoses and only five (6%) false positives.

The most striking feature of the scan appearances at 24 h was the absence of activity within the colon, only 28 (19%) of the 147 patients showing any activity within the large bowel, and of these 19 were localized to the caecum and ascending colon.

Although the kidneys were never visualized, the presence of activity within the urinary bladder was noted in 58 cases (40%) (Fig. 2). To assess urinary excretion of ^{67}Ga after pretreatment with iron, 24 h urinary collections were made from 15 patients who had been pretreated with Jectofer. The mean excretion of ^{67}Ga in these patients was found to be 16% of the injected dose in the first 24 h, these figures covering a very broad range (0.5%–41%). When these figures were examined in conjunction with the scan findings, we noted that all the patients with a low urinary excretion of ^{67}Ga had large lymphoma masses which avidly accumulated ^{67}Ga.

Discussion and Conclusions

All the scans performed after preloading with 100 mg Jectofer showed a different pattern of ^{67}Ga distribution at 24 h from the normally-accepted 72 h scan appearance and the seldom performed 24 h appearance. As predicted by recent animal work, Jectofer enhanced incorporation of ^{67}Ga citrate into


A FIG. 3. B

(A) Anterior view of a patient at 24 h, showing no abnormal localization of ^{67}Ga. There is a diffuse widening of the mediastinum which by 48 h (B) appears normal. Note the presence of activity within the bladder at 24 h in an otherwise clear abdomen. At 48 h (B) the bladder is not visualized but the familiar problem of activity within the colon is evident.

the skeleton (Hammersley and Taylor, 1980) and lowered the soft-tissue background uptake, but did not interfere with tumour uptake or scan interpretation.

At 24 h, interpretation of the scan in the abdomen and pelvis was much easier as very little, if any, of the ^{67}Ga had reached the colon. The recognition of any pathological uptake was much simpler and when large lesions were present in the abdomen, activity in the liver was always much lower than normal. This feature helped to distinguish lesions from colonic uptake, the ^{67}Ga apparently accumulating in these lesions in preference to the liver. We believe that preloading with iron may not greatly influence ^{67}Ga excretion into the colon but that it reduces the soft-tissue background making the abdominal structures more clearly seen at 24 h before appreciable activity has reached the colon. As a result any pathological accumulation is clearly demonstrated.

The broad, active, mediastinum seen at 24 h was the primary cause of the false-positive results in our series, and interpretation of the mediastinum and the root of the neck should be approached with caution. If it is uniformly widened with no irregularities, these appearances are probably normal, presumably due only to the high activity within the vascular component of the mediastinum.

All the pathological lesions we diagnosed in the mediastinum were within an irregularly widened mediastinum. However, small groups of nodes may be obscured by the broad vascular mediastinum and this occurred twice in our series. Re-examination of these doubtful cases at 48 h lowered the false-positive rate significantly as the high activity in the mediastinum had diminished by this time making diagnosis easier.

The urinary bladder was visualized in 40% of our cases in the absence of any pathological cause for this accumulation. This finding is of interest because when scanning is performed at 72 h the bladder is never seen. Reported figures for the excretion of ^{67}Ga citrate by the kidney during the first 24 h in the absence of Jectofer are in the range 2.7–35.2% (Zivanovic *et al.*, 1979). Since our figures fell within a broader range (0.5–41%) we are unable to say on the basis of the small number of patients studied to date whether or not urinary excretion is affected by Jectofer.

In conclusion, pretreating patients with 100 mg intramuscular Jectofer two hours before administering 55 MBq (1.5 mCi) ^{67}Ga citrate has made earlier imaging possible with no loss in diagnostic accuracy. It saves time because patients no longer have to wait 72 h between injection and scan, and reduces cost because for this earlier imaging only 55 MBq (1.5 mCi) instead of 92 MBq (2.5 mCi) of ^{67}Ga is required. Washout enemas to clean the colon are rarely required, thereby saving the patient unnecessary discomfort.

REFERENCES

HAMMERSLEY, P. A. G. and TAYLOR, D. M., 1980. The effect of the administration of iron on gallium 67 citrate uptake in tumours. *British Journal of Radiology, 53*, 563–571.

HOFFER, P. B., 1978. Mechanisms of localization. In *Gallium-67 Imaging*. Ed. P. B. Hoffer, C. Beckerman and R. Henkin (John Wiley and Sons, New York).

KING, D. J., DAWSON, A. A. and MACDONALD, A. F., 1980. Gallium scanning in lymphoma. *Clinical Radiology, 31*, 729–732.

SEPHTON, R. G. and DE ABREW, S., 1979. Effects of desferroxamine on ^{67}Ga distribution in tumour bearing mice. *Proceedings of the Society for Experimental Biology and Medicine, 161*, 402–406.

SEPHTON, R. and MARTIN, J. J., 1980. Modification of distribution of ^{67}Ga in man by administration of iron. *British Journal of Radiology, 53*, 572–575.

SMITH, F. W., DENDY, P. P., POCKLINGTON, T., DAWSON, A. A., FOSTER, M. A. and MALLARD, J. R., 1980. A preliminary investigation of ^{67}Ga-citrate distribution in hyperferraemic patients. *European Journal of Nuclear Medicine, 5*, 327–332.

TERNER, U. K., WONG, H., NOUGARON, A. A., LENTLE, B. C. and HILL, J. R., 1967. ^{67}Ga and ^{59}Fe uptake in human melanoma cells. *International Journal of Nuclear Medicine and Biology, 6*, 23–28.

ZIVANOVIC, M. A., MCCREADY, V. R. and TAYLOR, D. M., 1979. The urinary excretion of gallium-67 in patients with neoplastic disease. *European Journal of Nuclear Medicine, 4*, 277–282

Book reviews

Atlas of the Human Brain for Computerized Tomography. By T. Matsui and A. Hirano, pp. ix+570, 1978 (Igaku-Shuin, New York), $61.00.
ISBN 0-89640-027-1

The atlas consists of photographs of various sections through formalin-fixed brains taken at similar intervals to those used in computed tomography and made parallel to the orbito-meatal line and at angles of 10°, 15°, 20°, 25°, 30°, 40°, 50°, 60°, 80°, 110° and 140° to it. The photographs are excellent, accurately labelled and accompanied by clearly labelled diagrams. Computed tomographic sections are also correlated on the 15° and 20° sections; unfortunately a few of these show artefacts and in a few others resolution is suboptimal. This, however, is a minor defect in a beautifully produced atlas based on painstaking work involving the sectioning of over 500 brains.

There is no anatomical description, the text being short and describing only the method of preparation of the specimen for photography. It is difficult to imagine why the authors included a large number of references on computed tomography not related at all to the text and indeed referring to body as well as cranial CT; if they are included as suggestions for further reading they would have been better grouped in a logical sequence rather than alphabetically. The book is well indexed and is recommended as a useful practical departmental reference book on cerebral sectional anatomy in multiple planes.

B. E. KENDALL.

Correlative Neuroradiology. Cerebral Angiography and Computed Tomography. By R. G. Quisling, pp.xiii+311, 1980 (John Wiley, Chichester/New York), £24·50.
ISBN 0-471-05737-1

This book demonstrates cerebral anatomy portrayed by neuroradiological procedures, mainly cerebral angiography and computed tomography, and correlates the features shown on the various studies. It is divided into five sections. The first deals with the technique and basic principles of the method; the other four deal logically with anatomical regions, viz: the supratentorial compartment, the posterior fossa, the tentorial incisura and the suprasellar region respectively. The normal anatomy, the distortions caused by mass lesions, the distribution of the blood vessels and the relationship of the blood supply to the origin of pathological processes are demonstrated.

The text is clear and lucid. The radiographs are excellent and clearly labelled; they are supplemented by labelled diagrams and accompanied by detailed captions so that the work could be used as an atlas. The references are well selected and there is a good index.

The book demonstrates an excellent approach to neuroradiology and is particularly recommended to radiologists training in the speciality and to all radiologists and neuroscientists who are interested in improving or refreshing their basic knowledge of the subject.

B. E. KENDALL.

1981, *British Journal of Radiology*, *54*, 403–407

MAY 1981

Synthetic porphyrins as tumour-localizing agents

By G. D. Zanelli, Ph.D. and A. C. Kaelin, M.Sc.

Radioisotopes Division, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ

(*Received September 1980 and in revised form January 1981*)

ABSTRACT

A series of radioactively labelled porphyrin analogues have been synthesized and compared for tissue distribution and tumour uptake against ^{67}Ga in the same tumour-mouse system. The compounds were: ^{14}C-ms-tetraphenylporphine sulphonate (^{14}C-TPPS), ^{35}S-ms-tetraphenylporphine sulphonate (TPP^{35}S), ^{35}S-ms-tetra[β-naphthyl]porphine sulphonate (TNP^{35}S), ^{14}C-ms-thienylphenylporphine sulphonate (^{14}C-TTPPS) and ^{35}S-ms-tetra[p-tolyl]porphine sulphonate (TTP^{35}S).

^{14}C-TPPS and TNP^{35}S appear to concentrate in tumours to a greater extent than ^{67}Ga (ratios of tumour uptake for TPPS/^{67}Ga and TNPS/^{67}Ga were about two and three respectively) but their uptake in kidneys and lungs was also greater than that of gallium. The type of side group attached to the central tetrapyrrole ring appears to have a substantial effect on the tumour-localizing properties of these compounds.

Comparison of ^{14}C and ^{35}S-labelled TPPS indicates that the sulphonate groups are split off *in vivo* and that compounds with highly aromatic side groups (*e.g.* TNPS) and a radioactive label in a non-labile part of the molecule (*e.g.* in the tetrapyrrole ring system itself) would show even better tumour localization.

The feasibility of synthesizing porphyrins with a variety of reactive side groups suggests that it may be possible to introduce suitable γ-emitters while retaining the tumour-localizing properties.

It has been known for a long time that parenterally administered haematoporphyrin produces an intense fluorescence which appears to be restricted largely to malignant tissues. Experiments in transplanted tumours (Lipson *et al.*, 1961) and human neoplasms (Kelly *et al.*, 1975) seemed to confirm the tumour-localizing properties of haematoporphyrin. During the past decade there have been several reports on the exploitation of the fluorescent and photosensitizing properties of porphyrins for the localization (Profio and Doiron, 1977) and phototherapy (Diamond *et al.*, 1972; Kelly *et al.*, 1975) of human and experimental animal tumours.

In 1962 Winkelman prepared the synthetic prophyrin meso-tetraphenylporphine sulphonate (TPPS). Spectroscopy of tissue extracts from tumour-bearing rats (Walker carcinosarcoma-256) injected intravenously with 10 mg TPPS showed that this compound localized preferentially in the tumours. Again using spectroscopic methods, Winkelman and Hayes (1963) found that the necrotic zones of the Walker-256 tumour contained much more endogenous porphyrin, as well as parenterally administered TPPS, than the viable regions. Subsequently Winkelman *et al.* (1967) synthesized ^{3}H, ^{35}S and ^{14}C-labelled TPPS and investigated the *in vivo* distribution of these compounds again in rats bearing the Walker-256 tumour. They found that whereas the ^{14}C counting of combusted tissues and chemical analysis gave quantitatively similar recoveries and tumour/tissue ratios greater than 1.0 up to 90 h following injection, the distribution of the ^{3}H label was very different, with tumour/tissue ratios much less than 1.0 for kidneys, liver and spleen. They concluded that ^{3}H was labile at the intracellular pH existing *in vivo* and could exchange with serum proteins and other molecules. The same authors commented that the ^{35}S in the sulphonic acid groups of TPP ^{35}S was also labile and did not appear to concentrate in tumours. Carrano (1976) investigated the uptake of ^{14}C-TPPS by a cultured cell line and concluded that this porphyrin penetrated the cell membrane and was associated with cytoplasmic macromolecules. Carrano *et al.* (1977) showed, by chemical extraction from tissue digests in a virus-induced mouse rhabdomyosarcoma, that TPPS could be recovered in greater amounts from the kidneys than from the tumours, thus contradicting the results of Winkelman *et al.* (1967). With a view to the possible use of TPPS for tumour imaging, several workers have investigated the tissue distribution of haematoporphyrin or TPPS with a radioactive metal ion such as ^{57}Co, ^{99}Tc^{m} and ^{109}Pd chelated in the central part of the tetrapyrrole ring (Winkelman *et al.*, 1964; Hambright *et al.*, 1975; Brown and Wellman, 1974). They found that these metalloporphyrins (haematoporphyrin or TPPS) failed to concentrate in tumours. The explanations put forward for this phenomenon all assume that the metal is removed from the porphyrin ring *in vivo*.

It is evident that many questions regarding the tissue distribution and tumour uptake of synthetic porphyrins remain unanswered. Spectroscopic determination of porphyrins in tissue extracts is cumbersome and not very reliable. To date only one report has appeared in the literature on the tissue distribution of ^{14}C-labelled TPPS in one animal-tumour system (Winkelman *et al.*, 1967). Furthermore, TPPS has not so far been compared with the best currently available tumour localizers, ^{67}Ga or

^{111}In-bleomycin, in terms of tissue distribution and tumour uptake.

If, as shown by Winkelman (1962), TPPS accumulates in tumours more selectively than haematoporphyrin, then there is the possibility that other synthetic porphyrins with different side groups attached to the central tetrapyrrole ring might exhibit even greater tumour specificity.

In all experimental work carried out to date, relatively large amounts of TPPS have been used (0.1 to 30 mg/kg, corresponding to 7–2000 mg in a 70 kg man). Porphyrins are photosensitizers and if they are to be useful as imaging agents the administered dose must be kept below that which leads to unacceptable reactions. A survey of the literature indicates that the maximum acceptable dose is not more than 5.0 mg in a 70 kg man or a few micrograms in a mouse.

In this communication the tissue distribution of ^{14}C- and ^{35}S-labelled synthetic porphyrins having different side groups attached to the central tetrapyrrole ring has been compared with the distribution of ^{67}Ga in the same mouse-tumour system.

Materials and Methods

Preparation of synthetic porphyrins

All porphyrins used in this work were synthesized using the method of Adler *et al.* (1967). This procedure consisted of reacting pyrrole with the appropriate aldehyde in the presence of propionic acid. Sulphonation of the parent porphyrins was, unless otherwise stated, carried out using the method described by Winkelman *et al.* (1967). Radioactive labels were introduced into the porphyrins using either ^{14}C-carbonyl-labelled benzaldehyde or ^{35}S sulphuric acid (The Radiochemical Centre, Amersham, Code SJ44). The technical details of the preparation of the porphyrins are beyond the scope of the present communication, but can be supplied on request.

The following porphyrins were synthesized (Fig. 1): ^{14}C-ms-tetraphenylporphine sulphonate (^{14}C-TPPS), ^{35}S-ms-tetraphenylporphine sulphonate (TPP^{35}S); ^{35}S-ms-tetra[β-naphthyl]porphine sulphonate (TNP^{35}S); ^{14}C-ms-thienylphenylporphine sulphonate (^{14}C-TTPPS) and ^{35}S-ms-tetra[*p*-tolyl]porphine sulphonate (TTP^{35}S). These were chosen because they represent a series of compounds with different electron donor/acceptor characteristics. The molecular weights of the parent (unsulphonated) compounds were checked by mass spectrometry and found to be consistent with the calculated values (TPPS=614; TNPS=814; TTPS=670).

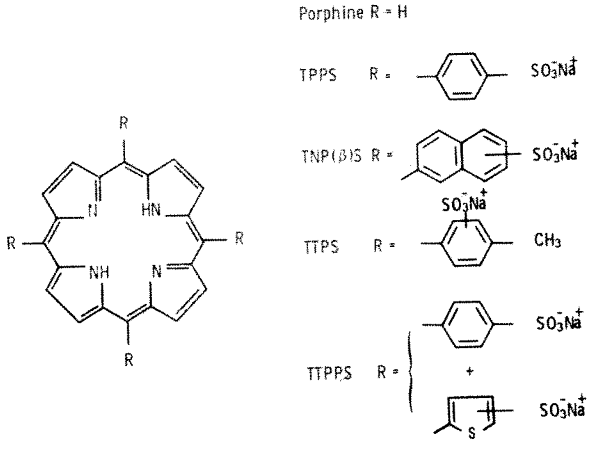


Fig. 1.

Structural formulae of the four porphyrin analogues used.

Animals and tumours

The tumour used throughout this study was a poorly differentiated carcinoma designated as "CBA Carcinoma NT" (Hewitt *et al.*, 1976) kindly supplied by Dr. H. B. Hewitt. Small fragments, less than 1 mm^3, were implanted in CBA mice under the skin in the sternal region. Two weeks later the tumours attained a mean diameter of approximately 7 mm and were used in experiments at this stage. The NT carcinoma has now been passaged 71 times in the local CBA mice without a single "no take" or spontaneous regression. Tumours of 7 mm average diameter do not show any evidence of gross necrosis but microscopic examination reveals the presence of small necrotic foci throughout the tumour mass.

Experimental procedures

For intravenous injections the mice were held in small, cylindrical wire cages and were not anaesthetized. All compounds were injected in one of the lateral tail veins in a volume of 0.1 ml using a 100 μl fixed-volume "Hamilton" syringe (Scientific Glass Engineering, Melbourne, Australia). The mice were killed by cervical dislocation at fixed intervals after injection and the tissues of interest removed. For the estimation of γ-emitting radionuclides the tissues were placed in pre-weighed polycarbonate tubes and counted in a LKB-Wallac autogamma counter (LKB Instruments Ltd., South Croydon, Surrey). The ^{14}C content of tissues was measured by combustion in a Tricarb sample oxidizer (Packard Instrument Company, Inc., Illinois, USA). In this case the tissues were placed

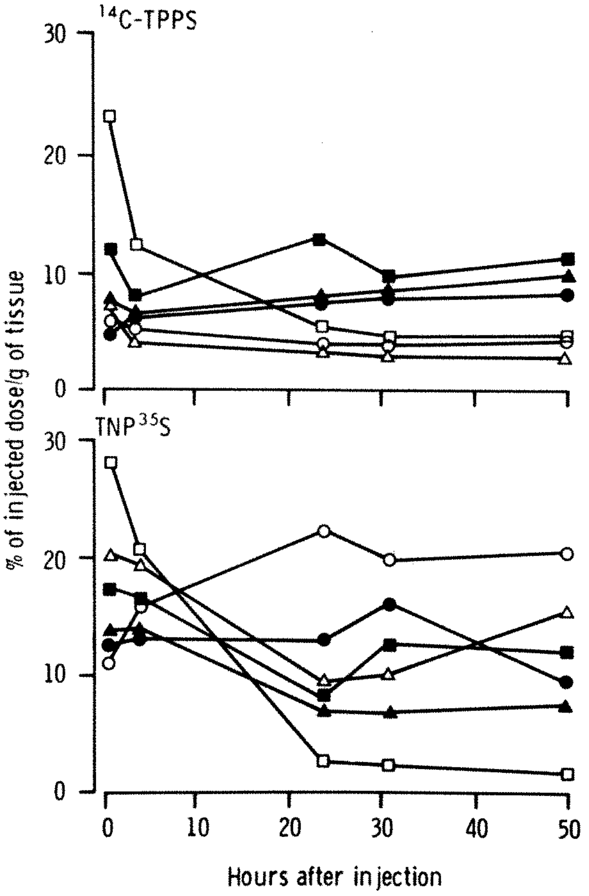


FIG. 2.

Uptake of ^{14}C-TPPS and TNP^{35}S (% of the injected dose/g of tissue) as a function of time after injection: ○—○ liver, △—△ spleen, □—□ blood, ▲—▲ kidneys, ■—■ lungs, ●—● tumour. The porphyrin dose was 20 μg.

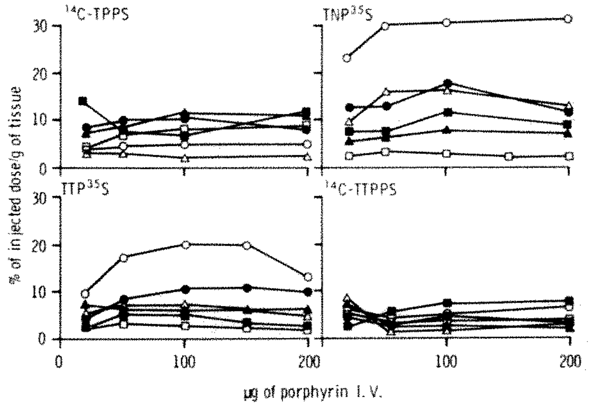


FIG. 3.

Percentage of the injected dose/g of tissue at 24 h as a function of dose (μg) for the four synthetic porphyrin analogues: ○—○ liver, △—△ spleen, □—□ blood, ▲—▲ kidneys, ■—■ lungs, ●—● tumour.

directly into pre-weighed combustion cups and weighed on a 0–500 mg torsion balance (White Electrical Instrument Co. Ltd., Worcestershire). ^{35}S was measured by placing the tissues into pre-weighed scintillation vials to which 6.0 ml of NCS solubilizer (Hopkins & Williams, Romford, Essex) were added. The vials were immersed in a water bath at 60°C and shaken at frequent intervals until the tissues were completely dissolved (48 to 60 h). Aliquots of 100 μl were then dispensed into fresh scintillation vials using a fixed volume "Finnpipette" with disposable tips (Jencons Scientific Ltd., Hemel Hempstead, Herts.) and 10.0 ml of scintillation cocktail added to each vial (100 g PPO, 2.27 g POPOP, 1.25 l Triton X-100, 2.5 l toluene).

In each experiment several standards consisting of 10% of the injected dose of the compound tested were counted alongside the tissue samples and the results were expressed as percentages of the injected dose per gram of wet tissue. The tissues investigated were tumour, liver, spleen, kidneys, lungs, stomach and duodenum, caecum and rectum, muscle, skin and blood. In the results each point represents the average for at least two mice. When ^{67}Ga (Code GJS2P, The Radiochemical Centre, Amersham) was used, it was mixed with the appropriate porphyrin immediately before injection.

RESULTS

Figure 2 shows the tissue distribution as a function of time after injection of 20 μg of ^{14}C-TPPS or TNP^{35}S. In Figs. 2–5 the uptake in only six of the ten tissues examined is shown for the sake of clarity. The percent uptake per gram of skin, muscle and gut was invariably of the order of 3% or less. The blood activity reached a low plateau by 24 h while at the same time the tumour uptake increased to a maximum. In one experiment the effect of increasing the time between injection and killing to five days was investigated, but it was found that the tumour uptake relative to that of other tissues did not improve after 24 h. A "standard" time of 24 h between injection and killing was therefore chosen for all subsequent experiments.

Figure 3 compares the relative tissue distribution of the four porphyrin analogues as a function of dose in the range 20 to 200 μg/mouse (0.66 to

6.6 mg/kg). Twenty micrograms was the lowest practical dose consistent with achieving reasonable counting statistics with these rather low specific activity compounds (20 μg of compound corresponded to 7–20 kBq (0.2–0.5 μCi) of either ^{14}C or ^{35}S). In most cases the highest tumour uptake was found at a dose of 100 μg, but the diminished uptake at the lower doses was not marked. It is also evident from Fig. 3 that there is a considerable difference in the tissue distribution of the four analogues. The highest tumour uptake occurs with the naphthyl analogue $TNP^{35}S$.

In Fig. 4 the tissue distribution of ^{14}C-TPPS is compared with that of TPPS having the radioactive label (^{35}S) in a much more labile position in the molecule. The ^{35}S-labelled porphyrin shows a lower concentration in the tumour and a much higher uptake in the liver, spleen and lungs than ^{14}C-TPPS. This supports the view of Winkelman *et al.* (1967) that the ^{35}S in the sulphonate groups is split off from the parent molecule *in vivo*. The results shown in Figs. 3 and 4 suggest that an even greater tumour uptake might be achieved with a naphthyl analogue labelled in a non-labile position—ideally in the tetrapyrrole ring system.

Figure 5 compares the tissue distribution of ^{67}Ga and ^{14}C-TPPS. The ^{67}Ga results are not significantly different from those reported by other investigators using different animal-tumour systems (Van Der Schoot, 1972; Lopez-Majano and Alvarez-Cervera, 1979). ^{14}C-TPPS (20 μg/mouse) shows a greater tumour concentration than ^{67}Ga, although its concentration in some normal tissues (kidneys and lungs) is also greater. Comparison of tumour uptake of ^{67}Ga with that of ^{14}C-TPPS (Fig. 5) and

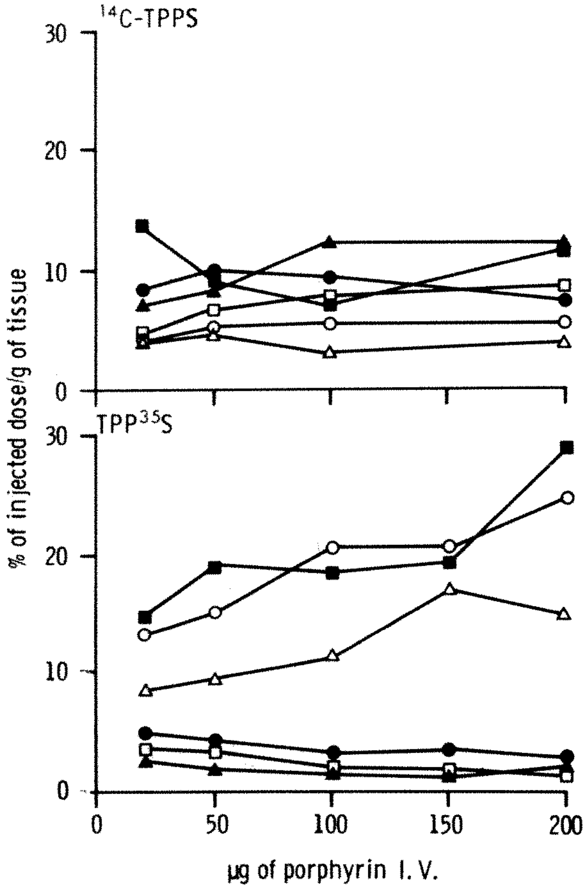


Fig. 4.

Comparison of the tissue uptake (% of the injected dose/g of tissue at 24 h) of ^{14}C-TPPS and $TPP^{35}S$ as a function of dose (μg): ○—○ liver, △—△ spleen, □—□ blood, ▲—▲ kidneys, ■—■ lungs, ●—● tumour.

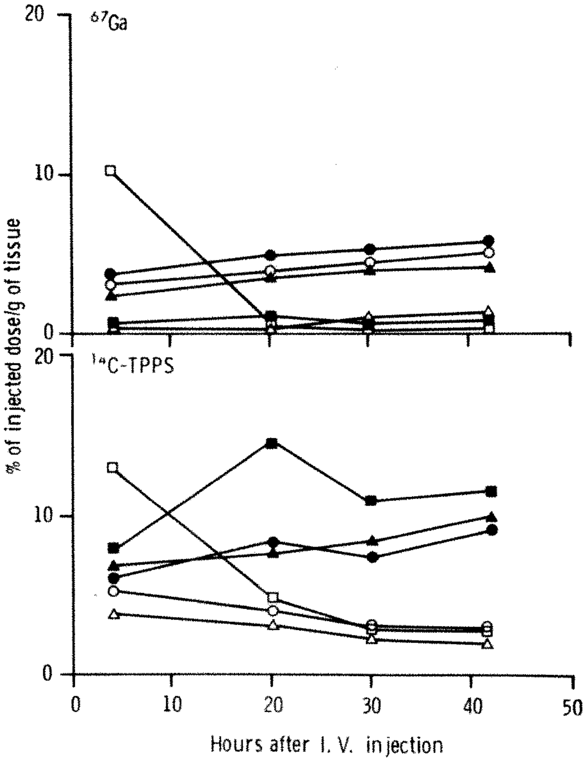


Fig. 5.

Comparison of the tissue uptake (% of the injected dose/g of tissue) of ^{14}C-TPPS (20 μg) and ^{67}Ga (75 kBq, 2 μ Ci) as a function of time after injection: ○—○ liver, △—△ spleen, □—□ blood, ▲—▲ kidneys, ■—■ lungs, ●—● tumour.

TNP^{35}S (Figs. 2 and 3) shows that the ratio of uptake in tumour for ^{14}C-TPPS/^{67}Ga is about 2.0 and that for TNP^{35}S/^{67}Ga is about 3.0.

DISCUSSION

The results indicate that the nature of the side groups affects the distribution of radioactivity among the various tissues. The more aromatic side groups appear to increase the tumour selectivity of these compounds, so on this basis one might expect 3-ring aromatic compounds such as anthracene or phenanthrene to improve the tumour-localizing properties even further.

One important problem which remains unsolved concerns the *in vivo* fate of the side groups. The results shown in Fig. 4 and the work of other authors (Winkelman *et al.*, 1964) suggest strongly that the injected ^{35}S porphyrins lose at least some of their labile sulphonate groups fairly rapidly and that the tissue distributions reported for TPP^{35}S may in fact represent mainly the distribution of ^{35}S metabolites. Equally well, it may be that the whole of a side group is detached *in vivo* and that the results obtained may, at least in part, represent the distribution of side groups or fragments thereof. Taken together, the results in Figs. 3 and 4 suggest that a naphthyl analogue with a non-labile radioactive label would be worth investigating. To elucidate these possibilities it is desirable to have compounds with the radioactive label in the tetrapyrrole ring system itself.

The finding that the compound appears to lose all its affinity for tumours when the central portion of the tetrapyrrole ring is occupied by a metal ion has had an inhibiting effect on efforts to use porphyrins for tumour detection. However there remain numerous alternative possibilities involving the introduction of radioactive metals or halides by way of reactive side groups on the aromatic part of the porphyrin molecules. The results so far obtained indicate that further exploration is warranted with the object of finding an imaging agent which would be an improvement on the widely used ^{67}Ga.

ACKNOWLEDGMENTS

We would like to thank Dr. A. Lawson and Mrs. M. Daly of the Clinical Chemistry Division who carried out the mass spectrometry, Miss Usha Raval for her technical help and Dr. N. Veall for continued support of the project, helpful criticism and advice.

REFERENCES

Adler, A. D., Longo, F. R., Finarelli, J. D., Goldmacher J., Assour, J. and Korsakoff, L., 1967. A simplified synthesis for meso-tetraphenylporphin. *Journal of Organic Chemistry*, *32*, 476.

Brown, A. D. and Wellman, H. N., 1974. A method for the preparation of a ^{99m}Tc-hematoporphyrin derivative and its tissue distribution patterns (abstract). *Journal of Nuclear Medicine*, *15*, 480.

Carrano, C. J., 1976. Studies on meso-tetra (*p*-sulfophenyl) porphine as a tumour localizing agent. Thesis, Texas A&M University, Texas, USA.

Carrano, C. J., Tsutsui, M. and McConnell, S., 1977. Localization of meso-tetra (*p*-sulfophenyl) porphine in murine sarcoma virus-induced tumor-bearing mice. *Cancer Treatment Reports*, *61*, 1297–1300.

Diamond, I., McDonagh, A. F., Wilson, C. B., Granelli, S. G., Nielsen, S. and Jaenicke, R., 1972. Photodynamic therapy of malignant tumours. *Lancet*, *ii*, 1175–1177.

Hambright, P., Rawwaz, R., Valk, P., McRae, J. and Bearden, A. J., 1975. The distribution of various water soluble radioactive metalloporphyrins in tumour-bearing mice. *Bioinorganic chemistry*, *5*, 87–92.

Hewitt, H. B., Blake, E. R. and Walder, A. S., 1976. A critique of the evidence for active host defence against cancer, based on personal studies of 27 murine tumours of spontaneous origin. *British Journal of Cancer*, *33*, 241–259.

Kelly, J. F., Snell, M. E. and Berenbaum, M. C., 1975. Photodynamic destruction of human bladder carcinoma. *British Journal of Cancer*, *31*, 237–244.

Lipson, R. L., Baldes, E. J. and Olsen, A. M., 1961. The use of a derivative of hematoporphyrin in tumour detection. *Journal of the National Cancer Institute*, *26*, 1–11.

Lopez-Majano, V. and Alvarez-Cervera, J., 1979. Neoplasm localization with radionuclides. *European Journal of Nuclear Medicine*, *4*, 313–324.

Profio, A. E. and Doiron, D. R., 1977. Fluorescence bronchoscope for lung tumour localization. *IEEE Transactions on Nuclear Medicine*, *NS-24*, 521–524.

Van Der Schoot, J. B., 1972. Gallium 67, its tumour affinity and tumour specificity. *Radiologia Clinica Biologica*, *41*, 371–377.

Winkelman, J. 1962. The distribution of tetraphenylporphinesulphonate in the tumor-bearing rat. *Cancer Research*, *22*, 589–596.

Winkelman, J. and Hayes, J. E., Jun., 1963. Distribution of endogenous and parenterally administered porphyrin in viable and necrotic portions of a transplantable tumour. *Nature*, *30*, 903–905.

Winkelman, J., Rubenfeld, S. and McAfee, J., 1964. The metabolism and excretion of Co^{57} tetraphenylporphinesulfonate in cancer patients. *Journal of Nuclear Medicine*, *5*, 462–470.

Winkelman, J., Slater, G. and Grossman, Judith, 1967. The concentration in tumour and other tissues of parenterally administered tritium- and ^{14}C-labelled tetraphenylporphinesulfonate. *Cancer Research*, *27*, 2060–2064

1981, *British Journal of Radiology*, *54*, 408–412

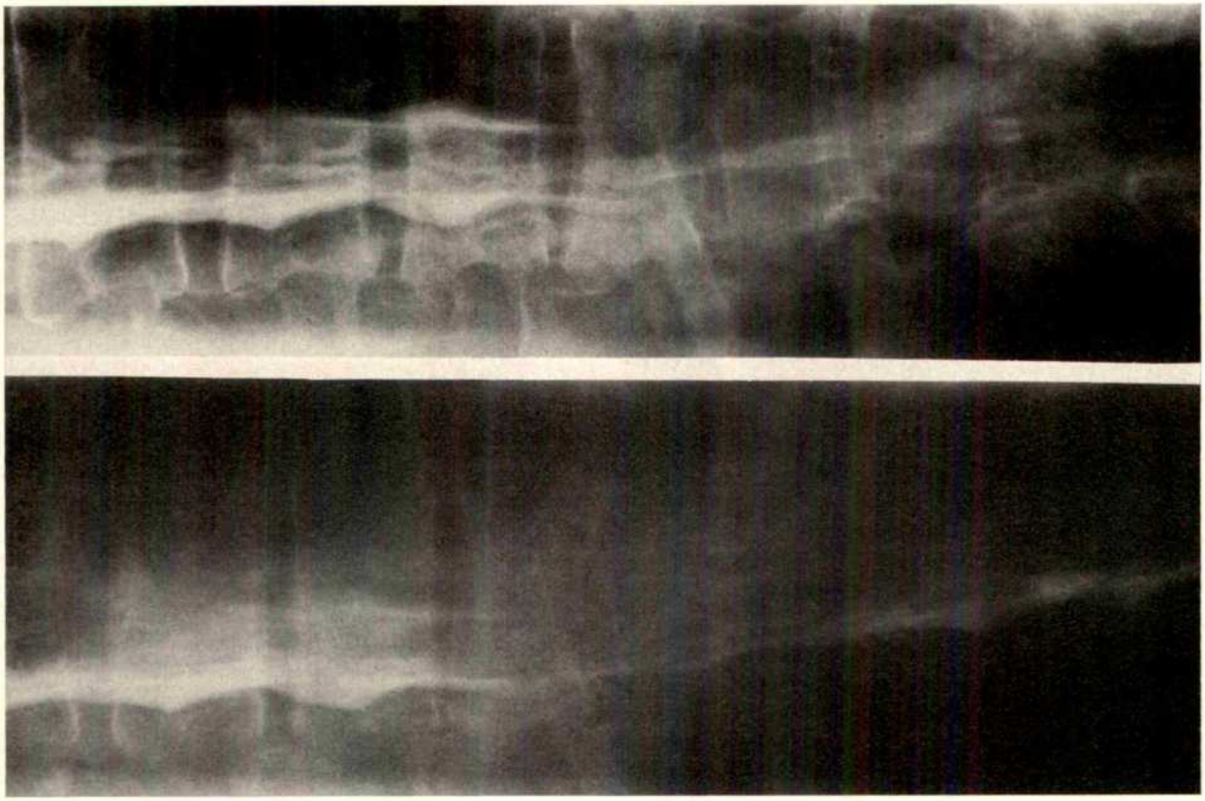
Technical notes

Myelographic study of the obstructed spinal theca with water-soluble contrast medium

By B. E. Kendall, F.R.C.P., F.R.C.R. and *A. R. Valentine, M.B., F.R.C.R., D.M.R.D.
Lysholm Radiological Department, National Hospital, Queen Square, London WC1

(*Received November 1980*)

Obstruction of the spinal theca which appears complete at the time of myelography is not usually absolute; if the upper part of the body is kept elevated, Myodil introduced above an obstruction will often have passed through by the next day. Also it is common observation that block is less frequent on lumbar myelograms performed with air than with Myodil. The latter has been assumed to be due to differences in surface tension effects of the media but the following explanation is more likely. When an injection is made below an obstruction, the subarachnoid space is expanded; at first this is compensated by compression of the epidural veins, but eventually the fluid or air lying adjacent to the obstruction tends to squeeze cranially past it. Since contrast media are usually injected with the patient sitting or lying on a horizontal table so that the thoracic spine slopes to a level higher than the lumbar, heavy opaque medium accumulates in the lumbar region and unopacified cerebrospinal fluid



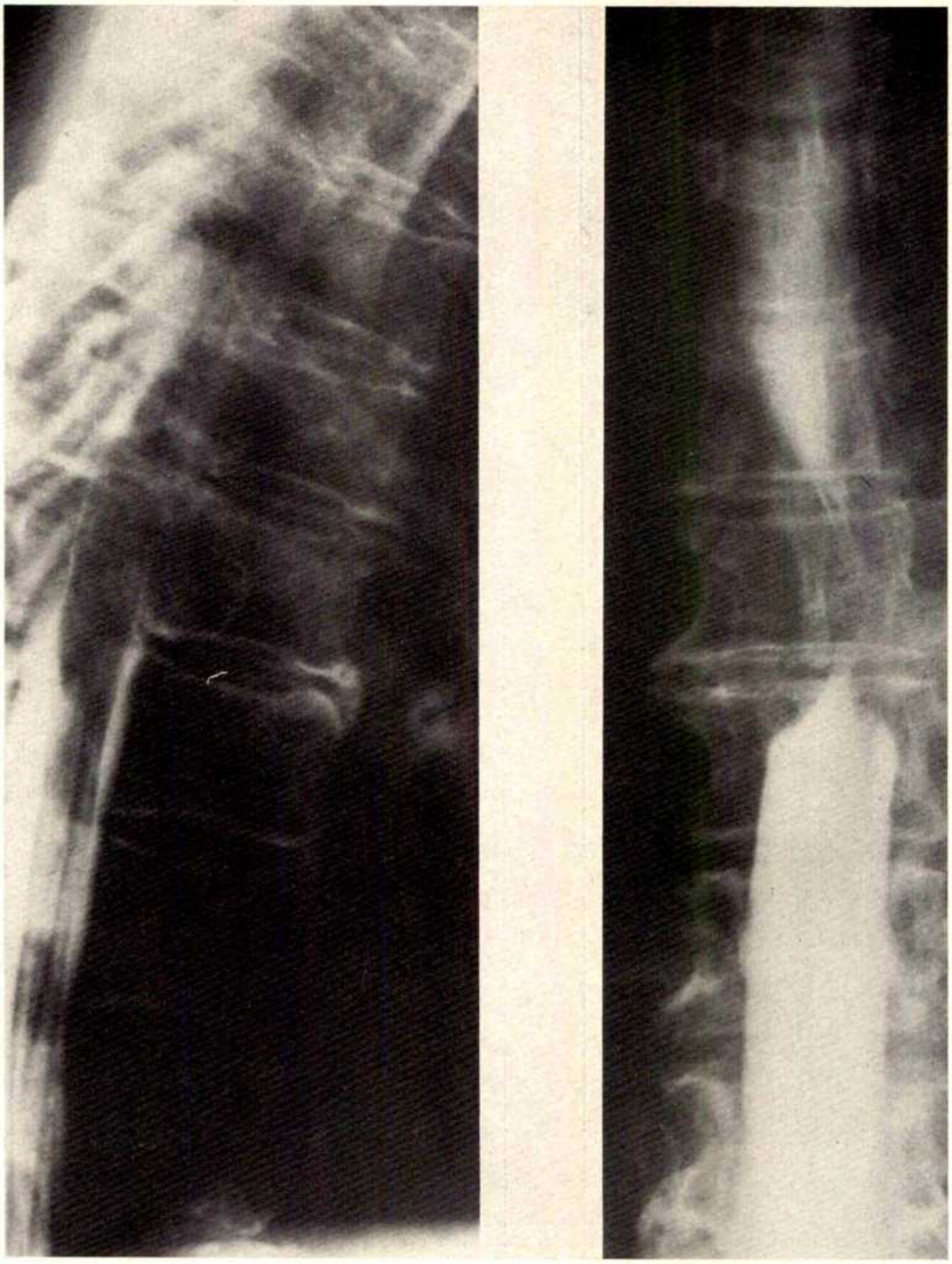
A (*above*) Fig. 1. B (*below*)

(A) Identifying the site of obstruction. The patient is lateral decubitus, table tilted head-down, AP radiography with horizontal beam.

(B) Continuing contrast injection. Note the lateral flexion of the spine which pools the contrast medium in the upper theca. See Fig. 5 (same patient) for clinical details.

---

*Present address: Royal Free Hospital, London NW3.



A FIG. 2. B

A 74-year-old female with progressive leg weakness and loss of bladder control. Five years previously a neurofibroma was removed from an intercostal nerve.

Clinical findings: Spastic paraparesis and sensory level at T8.

Radiology: (A) contrast medium sqeezing past obstructing lesion at D8. Note erosion of posterior aspect of vertebral body. (B) antero-posterior supine radiograph showing large right-sided extradural mass displacing the spinal cord to the left.

Operative findings: Extradural neurofibroma.

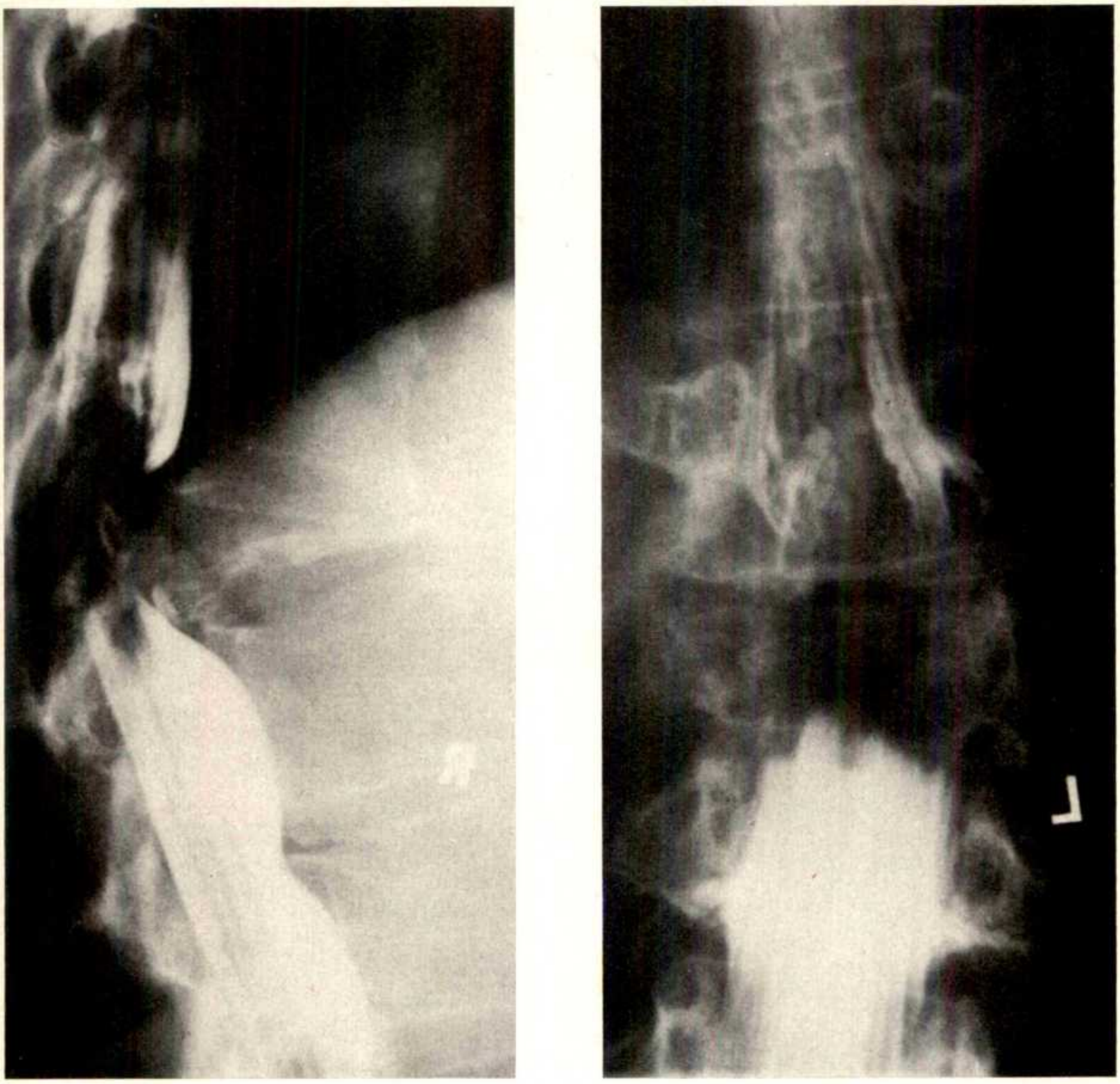


FIG. 3.

A 54-year-old female with back pain, progressive leg weakness and recent urinary incontinence. Mastectomy for breast cancer three years previously.
Clinical findings: Weakness and reduced tone in lower limbs.
Radiology: Plain radiographs demonstrated destruction and collapse of T12 with a localized paraspinal mass.
(A) considerable posterior displacement of the theca.
(B) contrast outlining upper and lower aspects of block. There are dilated veins in the lower thoracic theca.
Operative findings: Metastatic carcinoma.

tends to pass through the block; conversely air, which is often used in relatively large volumes, rises to the block and tends to pass through it. The former situation is modified to advantage by injecting the patient positioned so that the site of obstruction is dependent and the opaque medium then runs up to the block (Fig. 1A). As the injection is continued some will tend to pass through and the spine above the obstruction is positioned to pool it (Fig. 1B).

A method based on this principle but differing in detail was discussed by Levine and Olmstead (1979). They used Pantopaque in non-traumatic cases to

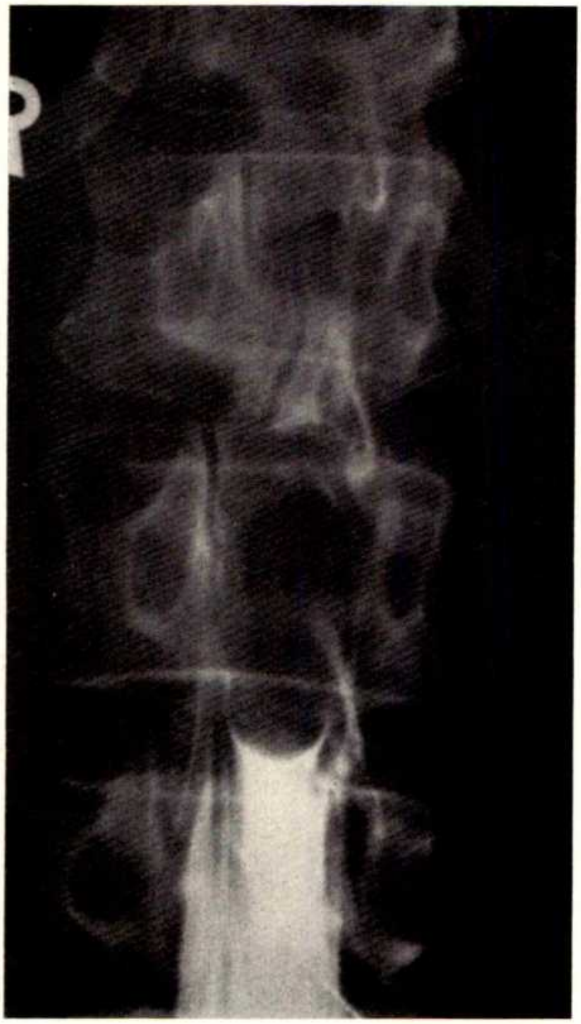


FIG. 4.

A 52-year-old male with a history of several months' increasing lower back and leg pain. Eighteen years previously an extradural meningioma was excised at D2.
Clinical findings: Leg weakness, brisk reflexes, bilateral extensor plantar responses.
Radiology: Shows the lower pole of an intradural mass at level L2/3 disc space. Note that there is sufficient contrast medium outlining the upper pole at L1/2 space to define the full extent of the mass.
Operative findings: Neurofibroma.

show a spinal block and then injected more Pantopaque or saline with the patient in Trendelenberg position. They demonstrated passage of the contrast medium through the obstructed segment in each one of a series of ten cases with no failures and no complications. They believe that the passage of the Pantopaque was caused by the second injection producing elevation of the intrathecal pressure greater than that usually occurring with contrast

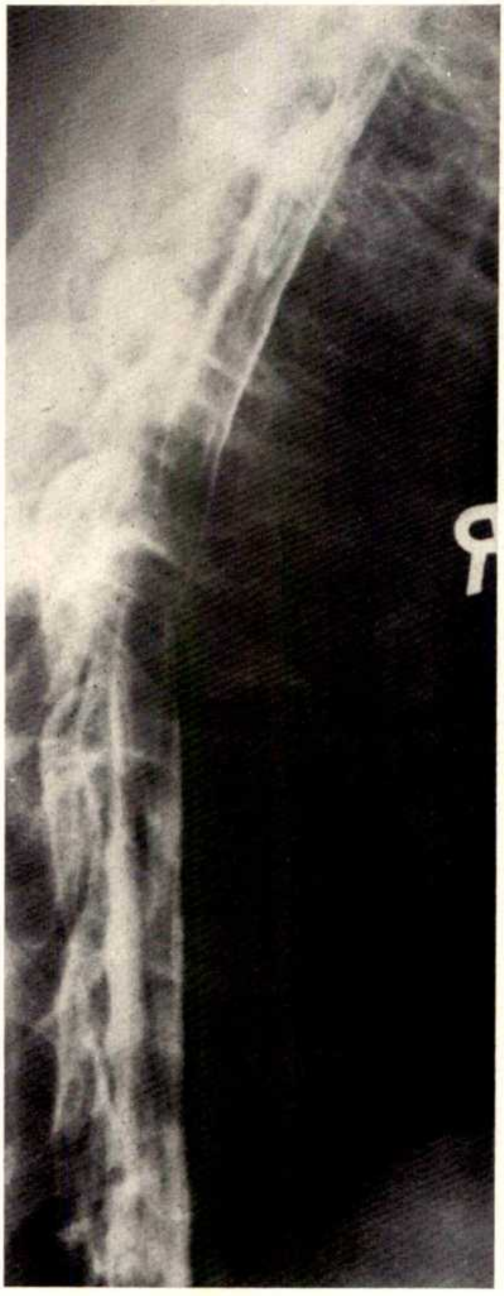


FIG. 5.

A 64-year-old male with a three-month history of back pain followed by leg weakness and urinary retention.
Clinical findings: Febrile and nauseated. Left leg weakness, severe dorsal column loss and an ill-defined sensory level at the costal margin.
Radiology: Plain films showed wedging of T8, and patchy sclerosis of T5. There is extensive thecal constriction (note displacement away from vertebral bodies) in addition to the more focal compression at T5.
Operative findings: Extensive extradural (streptococcal) abscess.

injection, and also considered that the method would not be useful for myelography with water soluble contrast media.

METHOD

Metrizamide in concentration 280–300 mg I/ml is injected into the lumbar theca through a 22-gauge needle, with the patient positioned lateral decubitus with the expected site of obstruction dependent but with the spine bowed so that the more cranial segments lie above the horizontal. The contrast medium is injected slowly under screen control so that the obstruction is immediately apparent and the table tilt can be adjusted to pool the contrast medium around it (Fig. 2A). On completion of the injection, lateral and anteroposterior decubitus radiographs are made; the patient is next positioned supine, if the obstruction is in the dorsal region (Fig. 2B), or prone, if it is in the cervical region, for further projections as indicated.

Before the procedure became routine, intrathecal pressures were measured during injection and did not rise above 210 mm water. This is well below the pressures which may be recorded during Queckenstedt and may therefore be considered safe (Shapiro, 1975).

RESULTS

This method has now been used in a large number of patients; the upper and lower border of the lesion causing partial obstruction was always adequately demonstrated (Figs 3, 4) and not infrequently some contrast medium was trapped alongside the lesion giving further anatomical information (Fig. 5). Most patients were unaware of the injection but occasionally there was relatively minor discomfort. In no case was there any increase in disability related to the procedure.

DISCUSSION

Metrizamide, being spontaneously resorbed, is particularly suitable for examination of patients with obstructing lesions; if oil is used above an obstruction it is retained. Obstructing lesions not infrequently present as emergencies and examination of these relatively difficult patients may then be conducted by radiologists with limited experience of cervical puncture. The examination performed as described is safe and simple and, in our experience, invariably successful in delineating the extent of an obstruction.

ACKNOWLEDGMENT

The authors gratefully acknowledge the secretarial assistance of Mrs. Amanda Pink.

REFERENCES

LEVINE, H. L. and OLMSTEAD, E. J., 1979. Myelographic evaluation of non-traumatic spinal canal obstruction: a new approach. *American Journal of Roentgenology*, *133*, 715–718.

SHAPIRO, R., 1975. *Myelography*, 3rd Edit. (Year Book Medical Publishers, Chicago), p.466.

Improved radiotherapeutic technique for prophylaxis of the central nervous system in patients with acute lymphoblastic leukaemia

By M. Pla, M.Sc., E. B. Podgorsak, Ph.D., T. H. Kim, M.D. and C. R. Freeman, M.B., B.S.

Department of Radiation Oncology, McGill University, Montreal, Quebec, Canada

(*Received January 1980 and in revised form November 1980*)

The importance of prophylaxis of the central nervous system (CNS) in the management of acute lymphoblastic leukaemia is well recognized. Radiotherapy reduces the incidence of CNS relapse from 40–60% to less than 10% (Dritschilo *et al.*, 1976; Evans *et al.*, 1970; Hustu *et al.*, 1973; MRC, 1973; Price and Johnson, 1973). Adequate coverage of the whole meningeal surface of the brain is essential and, since the retro-orbital tissues are also a potential site for relapse (Ridgeway *et al.*, 1976; Robb *et al.*, 1979), they should be irradiated to the same dose as the other parts of the CNS.

However, adequate irradiation of the retro-orbital tissues may produce a high dose to the lenses of the eyes, introducing a high risk of cataract formation. The ideal CNS prophylactic irradiation therefore includes the retro-orbital tissues but gives a low dose to the lenses of the eyes. This requirement demands a radiation beam with a clearly defined edge and a sharp dose gradient at the edge of the field—a requirement which is found in a number of situations in clinical radiotherapy. In these situations, a half-blocked beam may be the best means of achieving a sharp fall-off in dose. We have used the half-blocked technique in CNS prophylactic irradiation and in retinoblastoma, again to keep the dose to the lens as low as possible, and in the treatment of certain head and neck tumours. There are other instances where beam matching is more accurate if half-blocked beams are utilized. The purpose of this communication is to present physical data for half-blocked beams obtained on various supervoltage therapy units and to describe our technique for prophylactic irradiation of the central nervous system in patients with acute lymphoblastic leukaemia.

BEAM MEASUREMENTS

The half-blocked technique is used in our centre either on a cobalt unit* or a 4 MV linear accelerator†. Thus, most of the beam data presented are for these two units. We nevertheless add some 10 MV data‡ to show that the half-blocked field technique is also applicable to medium-energy accelerators. The properties of the half-blocked beams that were studied are the dosage profiles and the isodose distributions.

The beam profiles were measured with ion chambers in a water phantom and with TLD crystals in a specially constructed water phantom simulating the patient's head, and allowed us to study the dose levels in the vicinity of the lenses of the eyes during the prophylactic CNS irradiation. The isodose distributions were measured with a three-dimensional automatic isodose plotter|| and ion chambers§. A treatment planning computer¶ was used to determine the isodose distributions for the parallel opposed fields used for CNS irradiations.

In Fig. 1, the beam profiles for a 20 × 10 cm^2 half-blocked field are shown for the T-780 cobalt unit as well as for the T4 and Clinac-18 linear accelerators. The effective field size for the half-blocked field is 10 × 10 cm^2 with the beam edge much sharper on the central axis side than on the lateral border. If beam sharpness is defined as the width over which the profile at depth of dose maximum drops from 90% to 10%, then the sharpness on the central axis side is the same for all three supervoltage machines (7 mm) while the sharpness on the side away from the central axis varies from 2.5 cm for the cobalt unit (source diameter 1.5 cm) to 1.1 cm for the Clinac-18 accelerator. The solid lines in Fig. 1 represent profiles obtained with the three-dimensional isodose plotter and an ion chamber scanned through the beam at various depths (dose maxima, 4, 10, 15 and 20 cm) in a water phantom. The results of TLD measurements in the head phantom at depths of 4 and 10 cm (depths chosen to simulate the position of

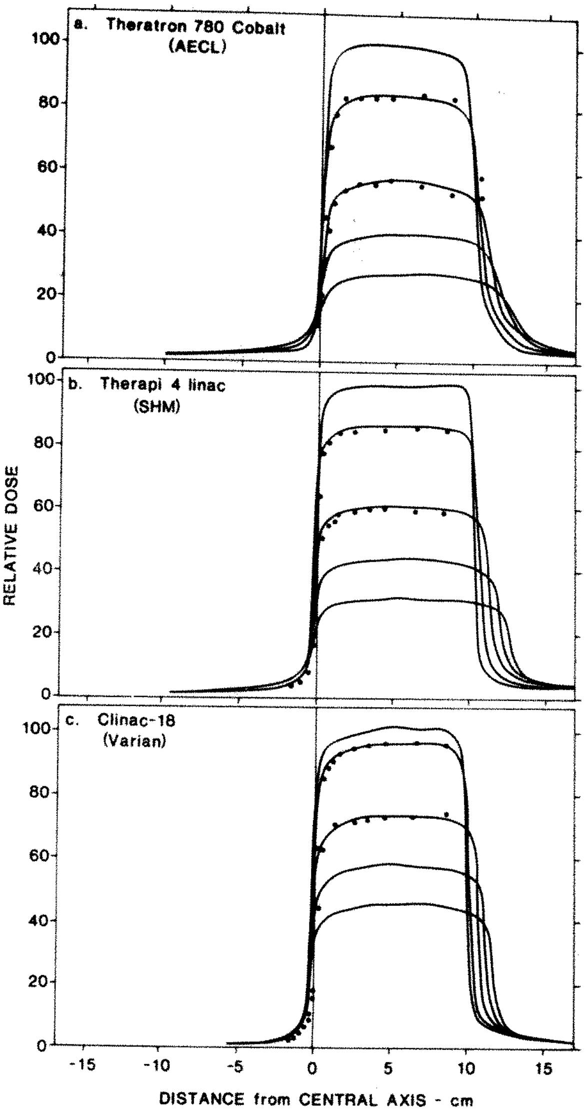


FIG. 1.

Half-blocked field profiles for various treatment units. Solid lines represent ionization chamber measurements at depths of dose maxima, 4, 10, 15 and 20 cm in water, while dots represent TLD data for depths of 4 and 10 cm in a water phantom.

---

*Atomic Energy of Canada, Ltd., Ottawa, Ontario; Theratron-780 cobalt unit.

†SHM Nuclear, Sunnyvale, California, Therapi 4 (T4) linac.

‡Varian Associates, Palo Alto, California: Clinac-18 accelerator.

||SHM Nuclear, Sunnyvale, California.

§Nuclear Enterprises, Beenham, Reading, England; Farmer Chamber 2505/3.

¶SHM Nuclear, Sunnyvale, California; Rad-8 treatment planning system.

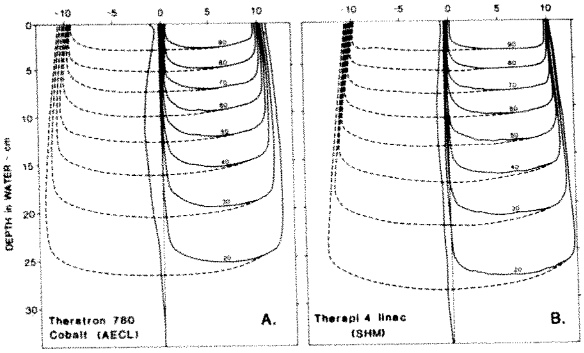


FIG. 2.

Isodose distributions for (A) a cobalt beam and (B) a 4 MV accelerator. Field size was 20 × 10 cm² at an SSD of 80 cm. Broken lines are for open beams and solid lines for a half-blocked beam.

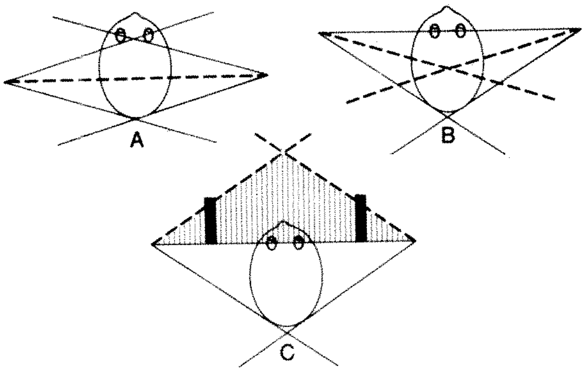


FIG. 3.

Radiation therapy methods for CNS prophylactic cranial irradiation. (A) parallel-opposed open fields with coincident central rays, (B) opposed open fields with coincident anterior beam edges, and (C) parallel-opposed half-blocked fields.

the eyes) are also shown in Fig. 1. The agreement between the ion chamber and TLD data is excellent.

The lead block used to shield half of the beam was 10 cm thick in order to decrease the primary beam transmission to less than 1%. The distance between the skin and the lead block was approximately 30 cm. The contribution of transmitted and scattered radiation under the lead block at distances of more than 1 cm from the central axis of the beam is of the order of 3% of the maximum dose.

Figure 2 shows isodose distributions for a 20 × 10 cm² half-blocked field at SSD 80 cm for a T-780 cobalt unit and a T4 linac. The open field isodose distributions are shown with broken lines for comparison. As shown before with profile data in Fig. 1, the beam sharpness on the central axis side of the half-blocked field is virtually the same for both the cobalt unit and the linac. It is only the 10% isodose line that spreads further under the blocked field for the cobalt unit, due to larger source size and increased side scatter. The penumbra on the lateral edge of the field is larger for the cobalt unit than for the linac, as expected.

THERAPEUTIC TECHNIQUE FOR CNS IRRADIATION

Lateral parallel-opposed fields achieve a uniform dose distribution throughout the cranial contents. However, when simple parallel-opposed lateral fields are used, the anterior border of each field must be far enough posterior to avoid irradiating the contralateral lens, and this will inevitably preclude adequate irradiation of the posterior orbit and retro-orbital tissues (Fig. 3A). One alternative is to angle both open beams posteriorly, matching the divergent beam edges anteriorly (Kline *et al.*, 1979) as shown in Fig. 3B. This technique enables the retro-orbital tissues to be adequately irradiated but the dose to the eye lens is high because of the large area of dose gradient at the beam edge due to the penumbra. To eliminate this problem, we have used half-blocked parallel-opposed fields with the central axis passing through the globe behind the lens (Fig. 3C).

Typical treatment plans for a patient treated with parallel-opposed beams on our 4 MV accelerator are shown in Fig. 4. The beams are positioned so that the 10% isodose line passes through the eye lenses. Comparison between the plain parallel-opposed plan (Fig. 4A), angled opposed plan (Fig. 4B) and the half-blocked parallel-opposed plan (Fig. 4C) shows that the latter gives the best sharpness. The distance between the 90% and 10% isodose lines for the half-blocked beams is 1 cm, as compared with 1.9 cm for the angled beams, and 2.2 cm for the simple parallel-opposed beams. Half-blocked beams are clearly superior to other techniques when sharp fall-off in dose is required.

The dose to the cranial contents with the half-blocked technique (Fig. 4C) is 24 Gy in ten days at the 97% isodose level, while the measured dose to the lens is of the order of 10% of the tumour dose or 2.4 Gy. The dose to the lens may be kept to the same order of magnitude using the alternative techniques (Fig. 4A and B) but the dose to the retro-orbital tissues will then be low and the risk of failure higher.

The set-up is simple and reproducible using the optical field localizer and the back pointer. Immobilization is usually by means of a head-rest only but localizing films taken during the course of treatment rarely show errors in positioning. Sedation may be necessary in young children.

We have used half-blocked beams for CNS irradiation regularly since 1976 and find it practical

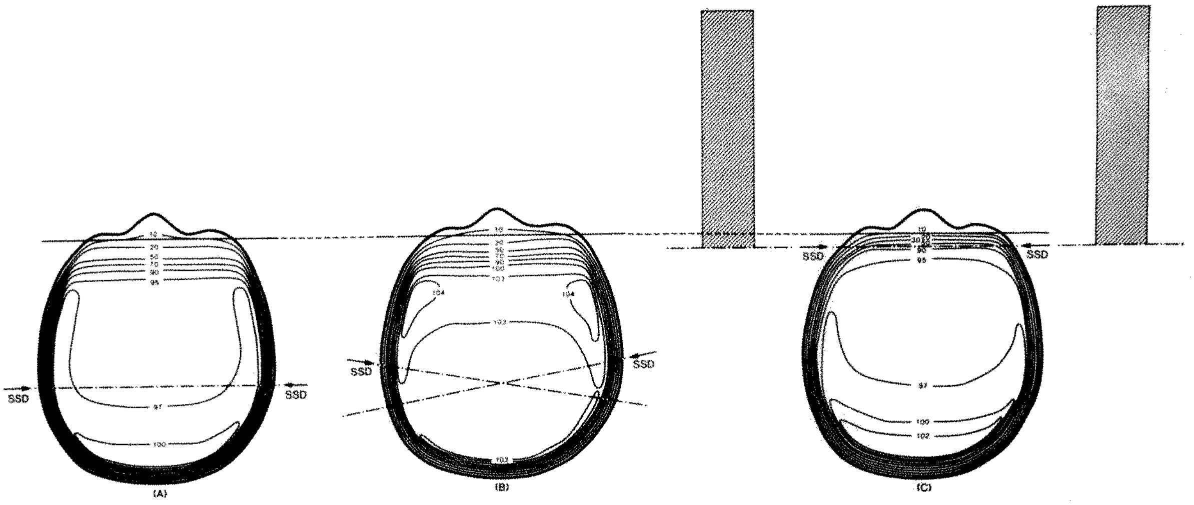


FIG. 4.

Typical cranial irradiation isodose distributions for a 4 MV accelerator. (A) Parallel-opposed open beams with coincident central rays, (B) opposed open beams with coincident anterior beam edges and (C) parallel opposed half-blocked beams.

and easily reproducible from day to day. As compared with our previous technique of simple lateral opposed fields, with which we found a 15% incidence of failure in the CNS and a 5% incidence of failure in the retro-orbital tissues, thus far we have seen no failures in the CNS or retro-orbital tissues, and no cataracts have been observed.

ACKNOWLEDGMENT

The authors wish to thank Prof. M. Cohen for helpful discussions during the preparation of this manuscript.

REFERENCES

DRITSCHILO, A., CASSADY, J. R., CAMITTA, B., JAFFE, N., FURMAN, L. and TRAGGIS, B., 1976. The role of irradiation in central nervous system treatment and prophylaxis for acute lymphoblastic leukaemia. *Cancer*, *37*, 2729–2735.

EVANS, A. E., GILBERT, E. S. and ZANDSTRA, R., 1970. The increasing incidence of central nervous system leukaemia in children. *Cancer*, *26*, 404–409.

HUSTU, H. O., AUR, R. J. A., VERZOSA, A., SIMONE, J. V. and PINKEL, D., 1973. Prevention of central nervous system leukaemia by irradiation. *Cancer*, *32*, 579–585.

KLINE, R. W., GILLIN, M. T. and KUN, L. E., 1979. Cranial irradiation in acute leukaemia: dose estimate in the lens. *International Journal of Radiation Oncology, Biology, Physics*, *5*, 117–121.

MEDICAL RESEARCH COUNCIL, 1973. Working party on Acute Lymphoblastic Leukaemia: Treatment of acute lymphoblastic leukaemia: effect of "prophylactic" therapy against central nervous system leukaemia. *British Medical Journal*, *ii*, 381–384.

PRICE, R. A. and JOHNSON, W. W., 1973. The central nervous system in childhood leukaemia: 1. The arachnoid. *Cancer*, *31*, 520–533.

RIDGEWAY, E. W., JAFFE, N. and WALTON, A. S., 1976. Leukaemia ophthalmopathy in children. *Cancer*, *38*, 1744–1749.

ROBB, R. M., ERVIN, L. D. and SALLAN, S. E., 1979. An autopsy study of eye involvement in acute leukaemia of childhood. *Medical and Pediatric Oncology*, *6*, 171–177.

1981, *British Journal of Radiology*, 54, 416–418

Case reports

An unusual case of neurofibromatosis: cystic bone lesions and coarctation of the aortic arch

By I. Beggs, F.R.C.R., M.R.C.G.P., D. G. Shaw, F.R.C.P., F.R.C.R., D. P. Brenton, M.D., F.R.C.P., and C. Fisher, M.R.C.Path.

University College Hospital, Gower Street, London, WC1

(Received October 1980)

We describe a case of neurofibromatosis with coarctation of the thoracic aorta and multiple cystic bone lesions.

Case Report

A 15-year-old caucasian girl was referred to University College Hospital following a fracture through a translucent lesion in her upper left fibula. Her mother was known to have neurofibromatosis and her brother had multiple cafe-au-lait spots. Her father was normal.

The patient was normally developed and had many cafe-au-lait spots and neurofibromata. A harsh late systolic murmur was present and radiated down the back of the spine. Her blood pressure was normal. Coarctation of the aorta just distal to the left subclavian artery was confirmed at aortography and was subsequently resected. The ductus was not patent.

There were multiple lesions (Figs. 1 and 2) at the ends of the shafts of the distal femora and tibiae and in the proximal tibiae and fibulae. They were expanded and translucent, appeared loculated and had well-defined, sclerotic margins. A fracture line was still visible through the lesion in the proximal left fibula.

The lesion in the right fibular head was biopsied. Histological examination (Fig. 3) showed cellular fibrous tissue with scattered giant cells, iron pigment and minimal new bone formation. These features were consistent with a non-ossifying fibroma or a brown tumour of hyperparathyroidism. Normal biochemistry excluded the latter and a diagnosis of non-ossifying fibroma was made. There was no neurofibromatous tissue.

Discussion

The family history and the presence of multiple cafe-au-lait spots confirm the diagnosis of neurofibromatosis (BMJ, 1966).

Renal artery stenosis and coarctation of the distal aorta are recognized features of neurofibromatosis (Senning and Johannson, 1960; Mena *et al.*, 1973), but coarctation of the aortic arch is not. One case was reported (Neiman *et al.*, 1974) of co-existent neurofibromatosis, Turner's syndrome and coarctation of the aorta just distal to the left subclavian and in another (Rowen *et al.*, 1975), neurofibromatosis was accompanied by multiple vascular abnormalities including coarctation of the thoracic and abdominal aorta. The thoracic coarctation, which was just distal to the left subclavian artery, was surrounded by neurofibromatous tissue.

In our case, the coarctation was at a similar site. There was no neurofibromatous tissue and we consider the relationship to be uncertain.

A relatively small number of cases of "cystic" bone lesions in neurofibromatosis has been reported. The term "cystic" has been used descriptively without

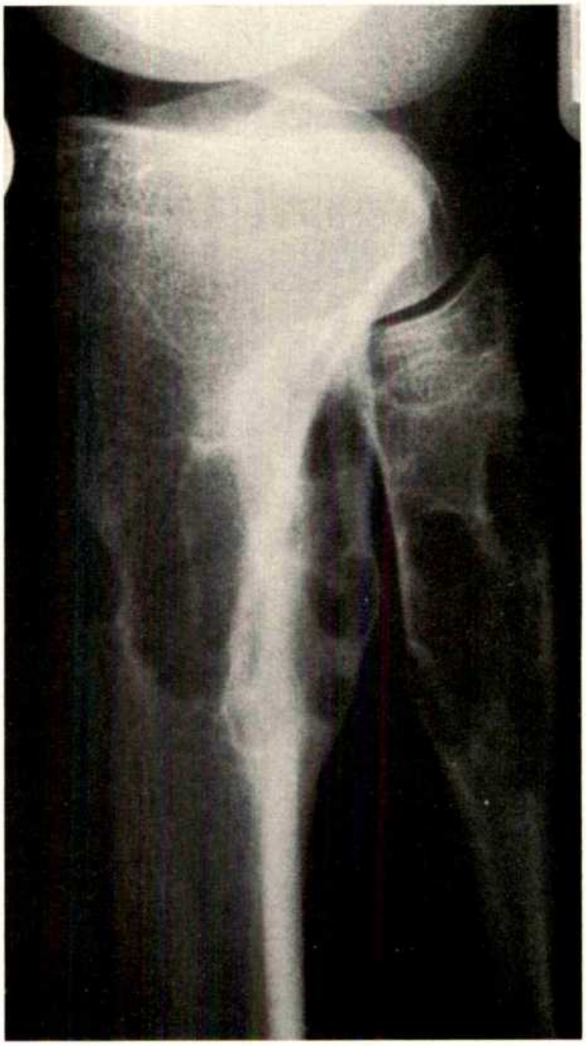


Fig. 1.

Several expanded "cystic" lesions in upper right tibia and fibula.

regard for histology; and some lesions were not illustrated or biopsied. Opinions as to the nature of the lesions and of their existence have varied. Two types of cystic abnormalities have been described: subperiosteal and intraosseous.

A sub-periosteal neurofibroma may excavate the outer cortex. Best known as rib notching, this can occur in long bones and may also be due to dysplastic periosteum (Klatte *et al.*, 1976). If the periosteum lays down new bone over the lesion a cystic appearance may result (Brooks and Lehman, 1924; McCarroll, 1950; Hensley, 1953; Hunt and Pugh, 1961; Sane *et al.*, 1971). Subperiosteal haemorrhage may produce a similar appearance (Hooper and McMaster, 1979). The existence and nature of this type of lesion is not questioned.

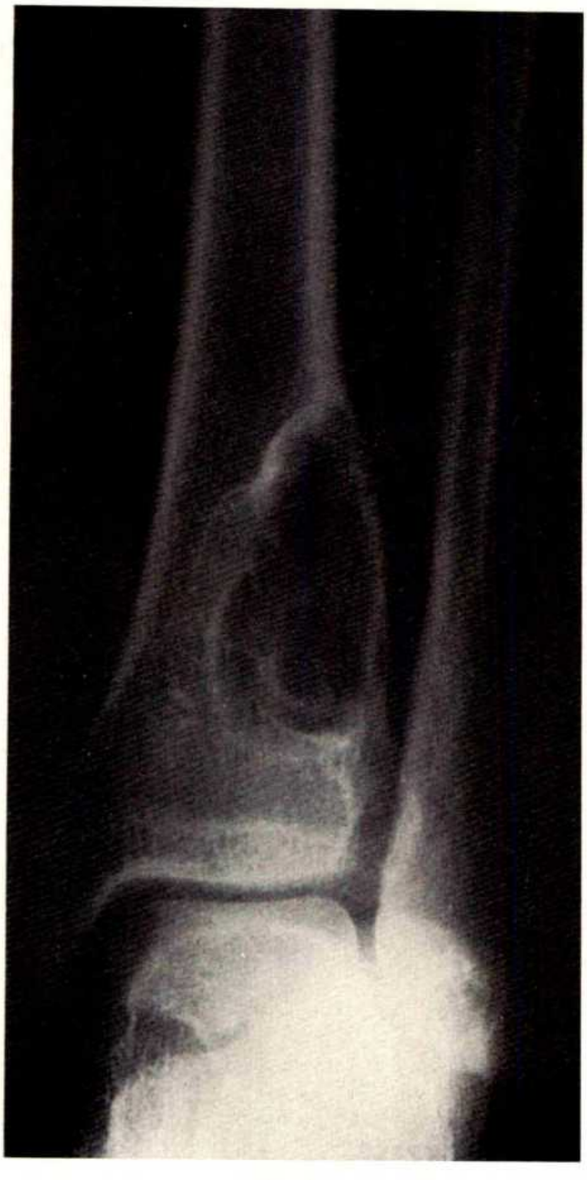


FIG. 2.
Expanded translucent lesion in lower left tibia.

The intraosseous lesion is more controversial. The existence of such lesions has been questioned. Hunt and Pugh (1961) and Holt (1978) declared them to be very rare. Their nature has also been problematical. "Cystic" lesions due to proven neurofibromatous tissue have been described (Friedman, 1944; Snyder *et al.*, 1974). Holt and Wright (1948) discussed two infants with multiple subcutaneous tumours and intraosseous bone lesions which resolved within a few months. Although they were biopsied and originally reported as cases of intraosseous neurofibromata, Holt (1978) later amended the diagnosis to multiple infantile fibromatosis. Jaffe (1958) considered whether multiple non-ossifying fibromata with brown skin patches might be a *forme fruste* of neurofibromatosis; but Goodnough *et al.*, (1975) decided that the presence of non-ossifying fibromata in neurofibromatosis was coincidental.

Opinion in recent years has therefore considered that translucent bone lesions in cases of generalized neurofibromatosis are rare and of doubtful significance but two reports have focused on a possible increased incidence of non-ossifying fibromata in neurofibromatosis. Mandell *et al.* (1979) reported nine cases of neurofibromatosis with "fibrous" lesions in the long bones of the leg very similar to those in our case and suggested that the presence of

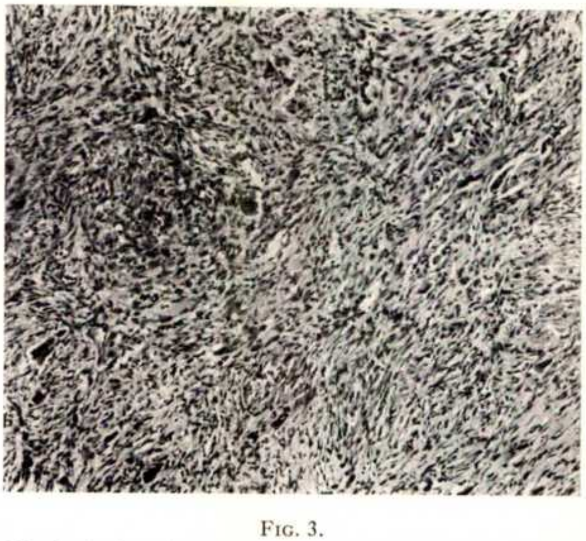


FIG. 3.
Histological specimen (haematoxylin and eosin × 100) from right fibula: cellular fibrous tissue with occasional giant cells.

1981, *British Journal of Radiology*, *54*, 418–420

multiple "fibrocystic" lesions about the knee should suggest the diagnosis of neurofibromatosis. None of these lesions was biopsied but they were considered radiologically to be a combination of fibrous cortical defects, non-ossifying fibromas and intraosseous neurofibromas. Holt (1980) reported conference discussions at which a number of cases of non-ossifying fibromata in neurofibromatosis were mentioned.

Our case had multiple translucent bone lesions, only one of which was biopsied. No neurofibromatous tissue was present and we assume that the histology, which showed a non-ossifying fibroma, was typical of the other lesions. This case supports the recent suggestion that there is an increased incidence of translucent intraosseous lesions in neurofibromatosis due to non-ossifying fibromas.

ADDENDUM

Since this paper was prepared, Schwartz and Ramos (1980) have reported a case of neurofibromatosis with similar cystic bone lesions due to non-ossifying fibromas.

REFERENCES

BMJ, 1966. Recognition of neurofibromatosis (leading article). *British Medical Journal*, *ii*, 1025–1026.

Brooks, B. and Lehman, E. P., 1924. The bone changes in Recklinghausen's neurofibromatosis. *Surgery, Gynecology and Obstetrics*, *38*, 587–595.

Friedman, M. M., 1944. Neurofibromatosis of bone. *American Journal of Roentgenology and Radium Therapy*, *51*, 623–630.

Goodnough, C. P., Kuhlmann, R. P. and Stark, E., 1975. Von Recklinghausen's neurofibromatosis with non-osteogenic fibroma. *New York State Journal of Medicine*, *75*, 2407–2409.

Hensley, C. D., Jnr., 1953. The rapid development of a "sub-periosteal bone cyst" in multiple neurofibromatosis. *Journal of Bone and Joint Surgery*, *35A*, 197–203.

Holt, J. F., 1978. Neurofibromatosis in children. *American Journal of Roentgenology*, *130*, 615–639.

1980. Pediatric radiology. In *The Year Book of Diagnostic Radiology*, Ed. W. M. Whitehouse. (Year Book Publishers, Inc., Chicago/London), p. 343.

Holt, J. F. and Wright, E. M., 1948. The radiological features of neurofibromatosis. *Radiology*, *51*, 647–664.

Hooper, G. and McMaster, M. J., 1979. Neurofibromatosis with tibial cyst caused by recurrent haemorrhage. *Journal of Bone and Joint Surgery*, *61A*, 274–275.

Hunt, J. C. and Pugh, D. G., 1961. Skeletal lesions in neurofibromatosis. *Radiology*, *76*, 1–20.

Jaffe, H. L., 1958. *Tumours and Tumourous Conditions of the Bone and Joints* (Kimpton, London), p.249.

Klatte, E. C., Franken, E. A. and Smith, J. A., 1976. The radiographic spectrum in neurofibromatosis. *Seminars in Roentgenology*, *11*, 17–33.

McCarroll, H. R., 1950. Clinical manifestations of congenital neurofibromatosis. *Journal of Bone and Joint Surgery*, *32A*, 601–617.

Mandell, G. A., Dalinka, M. K. and Coleman, B. G., 1979. Fibrous lesions in the lower extremities in neurofibromatosis. *American Journal of Roentgenology*, *133*, 1135–1138.

Mena, E., Bookstein, J. J., Holt, J. F. and Fry, W. J., 1973. Neurofibromatosis and renovascular hypertension in children. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *118*, 39–45.

Neiman, H. L., Mena, E., Holt, J. F., Stern, A. M. and Perry, B. L., 1974. Neurofibromatosis and congenital heart disease. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *122*, 146–149.

Rowen, M., Dorsey, T. J., Kegel, S. M. and Ostermiller, W. E., Jnr., 1975. Thoracic coarctation associated with neurofibromatosis. *American Journal of Diseases of Children*, *129*, 113–115.

Sane, S., Yunis, E. and Greer, R., 1971. Sub-periosteal or cortical cyst and intramedullary neurofibromatosis—uncommon manifestation of neurofibromatosis. *Journal of Bone and Joint Surgery*, *53A*, 1194–1200.

Schwartz, A. M. and Ramos, R. M., 1980. Neurofibromatosis and multiple non-ossifying fibromas. *American Journal of Radiology*, *135*, 617–619.

Senning, A. and Johansson, L., 1960. Coarctation of the abdominal aorta. *Journal of Thoracic and Cardiovascular Surgery*, *40*, 517–523.

Snyder, A. K., Proto, A. and Markarian, B., 1974. Osseous lesions in adolescence with known neurofibromatosis. *New York State Journal of Medicine*, *74*, 2401–2404.

A large bowel lymphoma complicating renal transplantation

By *D. N. M. Coggon, B.M., M.R.C.P., D. H. Rose, M.B., F.R.C.R. and I. D. Ansell, M.B., M.R.C.Path.

City Hospital, Nottingham

(*Received August 1980*)

The incidence of non-Hodgkin's lymphoma in renal transplant patients is more than 100 times expectation (Penn, 1977). In approximately half of such cases the central nervous system contains tumour, although many other organs may be involved less commonly. We report a case of large bowel lymphoma following renal transplantation, in which the radiological appearances were unusual.

CASE REPORT

A 47-year-old Indian with renal failure secondary to glomerulonephritis underwent cadaveric allograft renal transplantation in December 1976. Immunosuppression

---

*Present address: MRC Environmental Epidemiology Unit, Southampton General Hospital.

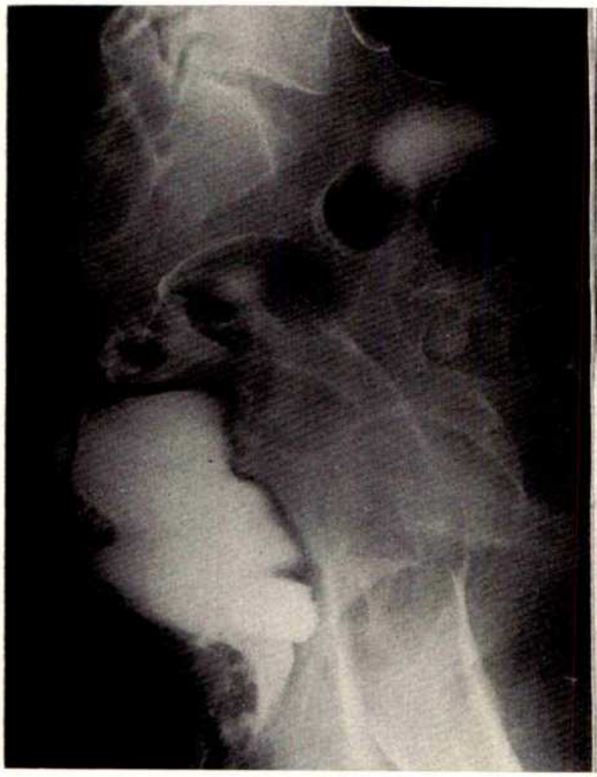


FIG. 1.

Lateral view of rectum. Multiple irregular ulcers in rectum and sigmoid colon.

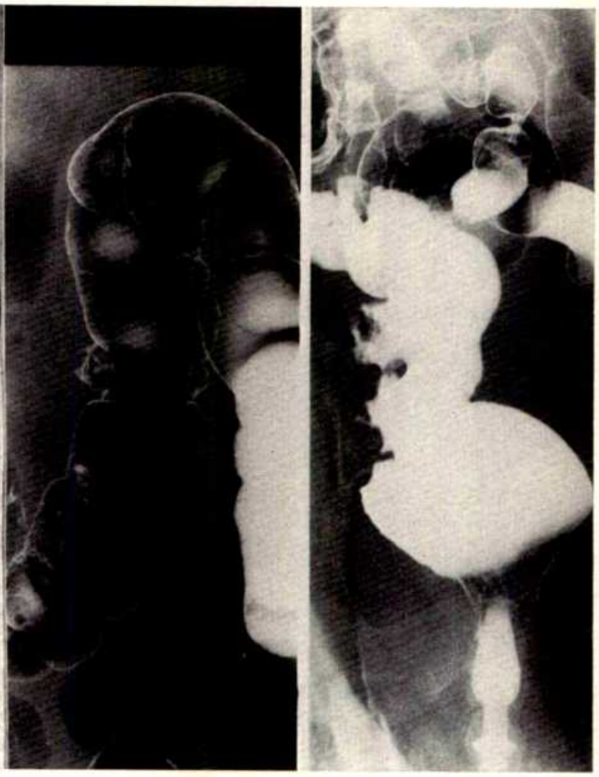


FIG. 2.

(A) Splenic flexure. (B) Oblique view of rectum.

comprized prednisolone 10–30 mg/day and azathioprine 2.0–2.5 mg/kg/day, with pulses of high dose methyl prednisolone for two early rejection episodes. He was well with good renal function when in April 1978 he developed anorexia, fever, lower abdominal pain and rectal bleeding necessitating transfusion. On sigmoidoscopy there was a lot of blood coming down from higher up the bowel, as a result of which the mucosa could not be adequately viewed.

Barium enema showed widespread ulceration throughout the large bowel, with normal intervening mucosa. Various sizes of ulcer were present. In the ascending colon there was a shallow plaque along the lateral wall whereas in the transverse and descending colon there were many small ring ulcers. In the rectum, sigmoid and distal transverse colon there were a total of five deep, punched-out, penetrating ulcers approximately 2 cm in diameter. They had shaggy irregular bases (Figs. 1 and 2). In several sites much smaller but similar lesions were present, particularly in the transverse colon. There was no evidence of perforation at the time of the enema.

Repeat sigmoidoscopy revealed a single fissuring ulcer, biopsy of which was suggestive of non-Hodgkin's lymphoma. The patient continued to bleed per rectum, but selective mesenteric angiography failed to localize the site of haemorrhage. He subsequently underwent left hemicolectomy, and shortly afterwards died as a result of Gram-negative septicaemia. Histological examination of the resected and autopsy specimens of bowel confirmed the presence of multiple punched-out ulcers throughout the colon and rectum, and these contained lymphoma cells in their bases. One of the ulcers had perforated. Small deposits of lymphoma were also found throughout the liver and in the brain.

DISCUSSION

Typically lymphomas of the colon and rectum take one of three forms (Glick and Soule, 1966; Wychulis *et al.*, 1966): diffuse infiltration of the bowel wall; single or multiple intraluminal polyps; or a circumscribed thickening of bowel wall, either plaque-like or annular. Barium enema is the investigation of choice for the pre-operative demonstration of such tumours (Ngan and James, 1973). In the series of Wychulis *et al.*, 54 out of 60 large bowel lymphomas were shown by this method, although most were misdiagnosed as carcinoma. The radiological appearances are pleomorphic and mirror the gross pathological findings described above. Most tumours simulate carcinoma, appearing on barium enema as intraluminal filling defects or as strictures. However, the strictures are said to be less rigid than in carcinoma and to have tapering at the end of the stenosis, rather than the shouldering which gives the characteristic apple-core appearance of carcinoma. In Wychulis's series ulceration and perforation of the colon were common, but this ulceration appeared mainly in large proliferative and infiltrative

1981, *British Journal of Radiology*, *54*, 420–422

lesions. Glick and Soule also report ulceration and varying degrees of extramural extension. The distribution of lesions in lymphoma is predominantly right-sided, the caecum being the site of lesion in 85% of the cases described by Glick and Soule. Occasionally the entire colon may be involved by lymphoma, producing either multiple small intraluminal polyps or a tubular large bowel.

The barium enema in our patient showed a different appearance from those described in the literature. There was widespread ulceration, but without any narrowing of the bowel lumen, and between ulcers the mucosa appeared completely normal. These most unusual appearances had not previously been encountered and we can find no cescription of such lesions in the literature. A single dase report (Pinkus *et al.*, 1974) describes two other patients with colonic lymphoma following renal transplantation. In one patient the tumour took the form of multiple ulcerating nodules, one of which had perforated. In the other, lymphoma cells were found in an abscess associated with diverticulitis. In addition to lymphoma other diagnoses which we considered on the basis of the barium enema included an atypical form of Crohn's disease, and, in view of the patient's racial origin, tuberculosis.

ACKNOWLEDGMENTS

We thank Professor R. W. Blamey and Dr. R. P. Burden for allowing us to present this case.

REFERENCES

GLICK, D. D. and SOULE, E. H., 1966. Primary malignant lymphoma of colon or appendix. Report of 27 cases. *Archives of Surgery (Chicago)*, *92*, 144–151.

NGAN, H. and JAMES, K. W., 1973. *Clinical Radiology of the Lymphomas* (Butterworths, London), p. 127.

PENN, I., 1977. Development of cancer as a complication of clinical transplantation. *Transplantation Proceedings*, *9*, 1121–1127.

PINKUS, G. S., WILSON, R. E. and CORSON, J. M., 1974. Reticulum cell sarcoma of the colon following renal transplantation. *Cancer*, 34, 2103–2108.

WYCHULIS, A. R., BEAHRS, O. H. and WOOLNER, L. B., 1966. Malignant lymphoma of the colon. A study of 69 cases. *Archives of Surgery (Chicago)*, *93*, 215–225.

Therapeutic embolization of phaeochromocytoma

By J. B. Timmis, M.B., B.S., M. J. Brown, B.A., M.Sc., M.R.C.P. and D. J. Allison, B.Sc., M.D., F.R.C.R.

Department of Diagnostic Radiology and Clinical Pharmacology, Hammersmith Hospital and Royal Postgraduate Medical School, Du Cane Road, London W12

(Received October 1980)

A patient with metastatic deposits from a phaeochromocytoma may present the clinician with a difficult management problem owing to the relative insensitivity of this tumour to available chemotherapeutic agents and radiotherapy. We report a case in which the adverse humoral effects produced by lymph node metastases from a urinary bladder phaeochromocytoma have been successfully controlled by means of therapeutic arterial embolization.

CASE REPORT

A 30-year-old caucasian man presented in 1978 with an 18-year history of headaches induced by micturition. He had severe hypertension (260/170 mm Hg) and his plasma noradrenaline concentration was grossly elevated at 58 ng/ml (normal range 0.15–0.8).

An intravenous urogram revealed a filling defect in the urinary bladder and the presence of a pelvic mass was confirmed by ultrasound and arteriography. Selective venous sampling demonstrated high noradrenaline concentrations in both internal iliac veins suggesting the diagnosis of phaeochromocytoma of the bladder. At laparotomy a tumour was found involving the bladder and adjacent to this were two other tumours, not seen by the pre-operative imaging techniques. A partial cystectomy was performed and all three tumours were sucessfully resected. Postoperatively the patient became asymptomatic and his blood pressure fell to 115/85 mm Hg. The plasma noradrenaline concentration one month later was 0.58 ng/ml.

In May 1980 his blood pressure was again found to be elevated (190/120 mm Hg), and the plasma noradrenaline concentration had risen to 34 ng/ml. An IVU showed no evidence of bladder tumour and selective venous sampling, lymphography and CT scanning indicated the presence of recurrent tumour in left-sided pelvic nodes. Pelvic arteriography from a percutaneous femoral approach showed the affected nodes to be supplied almost exclusively by the left fifth lumbar artery. Selective arteriography of this single feeding vessel revealed a rich tumour circulation (Fig. 1) and this was embolized using finely divided lyophilized human dura mater (Lyodura, Davis and Geck Ltd.). A post-embolization aortogram confirmed that the fifth lumbar artery had been completely occluded with abolition of the tumour circulation (Fig. 2). During the four weeks preceding the embolization, the patient had been treated with an α-adrenergic antagonist (oral phenoxybenzamine). Immediately prior to the study 5 mg of phentolamine were injected intravenously, and two 10 mg increments were administered during the procedure, maintaining the blood pressure between 105/70 and 170/110 mm Hg. Nitroprusside and plasma were available to control sudden fluctuations in arterial blood pressure, which was continuously monitored

---

Reprint requests: D. J. Allison.

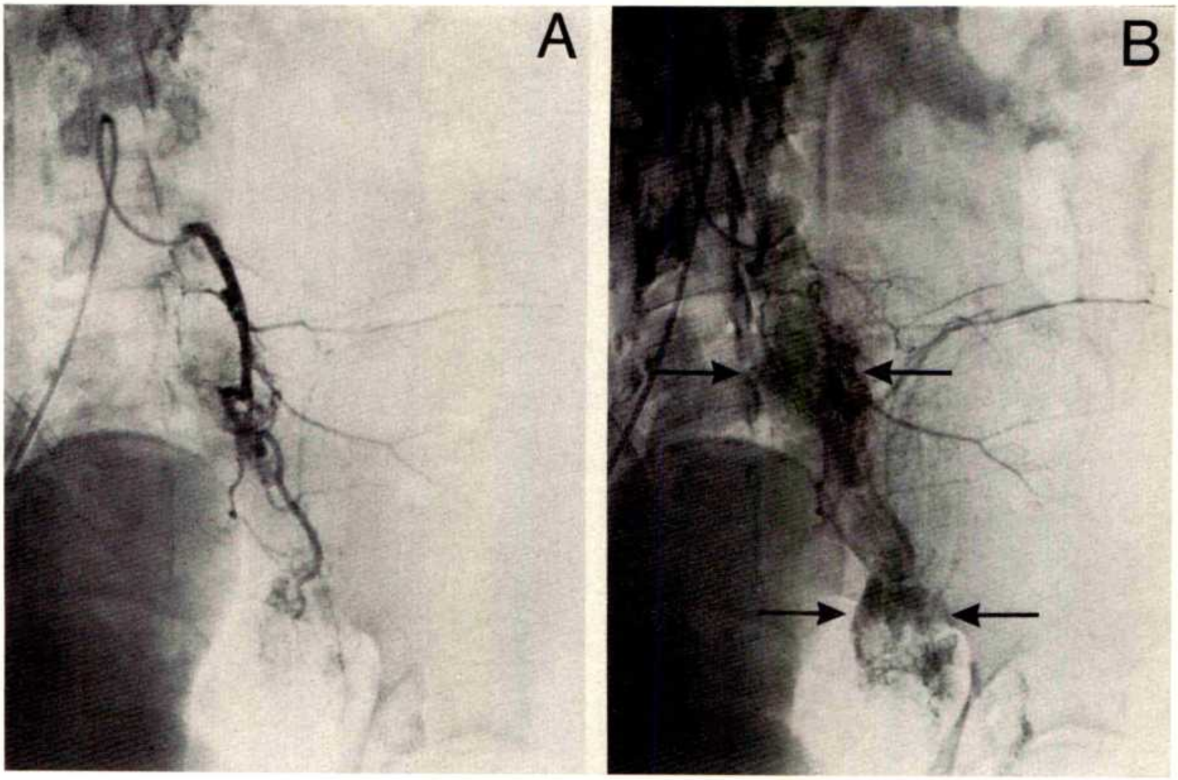


FIG. 1.

Arterial phase (A) and capillary phase (B) of selective left fifth lumbar arteriogram. The presence of recurrent tumour in the pelvic lymph nodes is indicated by the pathological circulation which is most conspicuous in the capillary phase (arrows).

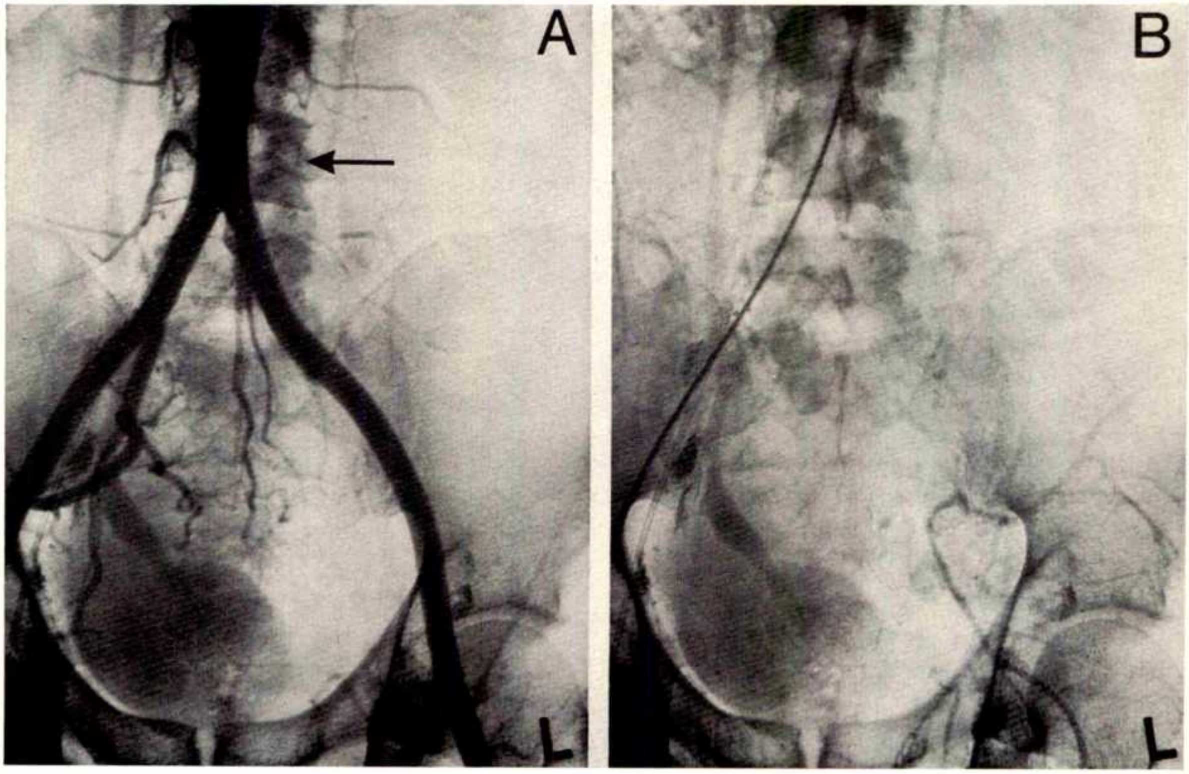


FIG. 2.

Arterial (A) and capillary (B) phases of a pelvic aortogram following embolization of left fifth lumbar artery (origin arrowed). The blood flow to the tumour deposits has been abolished.

1981, *British Journal of Radiology*, *54*, 422–423

by the Roche Arteriosonde; in the event they were not required. The plasma noradrenaline level rose transiently after the embolization to 112 ng/ml, but thereafter fell progressively to 8.2 ng/ml the following day and 6.9 ng/ml the following week. Six weeks later the noradrenaline level remained reduced at 6.9 ng/ml and the blood pressure was 114/78 mm Hg. Three months following the procedure the patient remains well on no medication.

DISCUSSION

Surgery remains the treatment choice for phaeochromocytoma since successful removal of the tumour can be achieved in the great majority of cases (Scott *et al.*, 1976; Modlin *et al.*, 1979). The management of metastatic recurrence from a malignant phaeochromocytoma, however, presents a more difficult management problem owing to the fact that these tumours are insensitive to chemotherapeutic agents (Remine *et al.*, 1974) and conventional radiotherapy, though doses in excess of 4000 cGy (rad) may be of value (James *et al.*, 1972).

In recent years the technique of therapeutic arterial embolization has been increasingly employed in the management of tumours both as a pre-operative manoeuvre to facilitate surgical resection, and as a palliative measure in inoperable cases (Allison, 1978). The technique has proved particularly valuable for controlling the humoral activity of malignant endocrine tumours, but has not to our knowledge been used previously in a case of metastatic phaeochromocytoma.

The primary tumour in our patient was situated in the urinary bladder, a rare but well-recognized site for phaeochromocytoma (Javaheri, 1975). The metastases arising from this neoplasm were situated in a chain of pelvic lymph nodes, and it was felt that the surgical removal of these deposits would not only present a difficult technical problem, but also would carry the risk of causing impotence in a relatively young man.

It is too early to assess the long-term value of the embolization technique in the present case, but it has effected successful biochemical and clinical control of tumour activity for three months, and the procedure can be repeated as required if there should be further evidence of tumour recurrence in a site accessible to the embolizing catheter.

ACKNOWLEDGMENTS

We would like to thank Professor C. T. Dollery and Professor R. B. Welbourn for permission to publish details of their patient.

REFERENCES

ALLISON, D. J., 1978, Therapeutic embolization. *British Journal of Hospital Medicine*, *20*, 709–714.

JAMES, R. E., BAKER, H. L., and SCANLON, P. W., 1972. The roentgenologic aspects of metastatic phaeochromocytoma. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *115*, 783–793.

JAVAHERI, P. and RAAFAT, J., 1975. Malignant phaeochromocytoma of the urinary bladder: report of two cases. *British Journal of Urology*, *47*, 401–404.

MODLIN, I. M., FARNDON, J. R., SHEPHERD, A., JOHNSTON, I. D. A., KENNEDY, T. L., MONTGOMERY, D. A. D. and WELBOURN, R. B., 1979. Phaeochromocytoma in 72 patients: clinical and diagnostic features, treatment and long term results. *British Journal of Surgery*, *66*, 456–465.

REMINE, W. H., CHONG, G. C., HEERDEN, J. A. VAN, SHEPHS, S. G. and HARRISON, E. G., 1974. Current management of phaeochromocytoma. *Annals of Surgery*, *179*, 740–748.

SCOTT, H. W., OATES, J. A., NIES, A. S., BURKO, H., PAGE, D. L. and RHAMY, R. K., 1976. Phaeochromocytoma. Present diagnosis and management. *Annals of Surgery*, *183*, 587–593.

Arteriography of Castleman tumour of the mesentery

By T. E. Gudmundsen, M.D. and A. Kolbenstvedt, M.D.

Department of Radiology, Rikshospitalet, The National Hospital, Oslo 1, Norway

(Received October 1980)

Giant lymph node hyperplasia (Castleman tumour) is a benign disease which has been divided into two histological types: the hyaline-vascular lesions which are most frequent, and the plasma-cell lesions which cause blood abnormalities such as anaemia, elevated sedimentation rate and hyperglobulinaemia (Keller *et al.*, 1972). Although most of the lesions are intrathoracic, a few with retroperitoneal (Tuttle and Shier, 1979) and pelvic (Riba, 1979) location have been reported. Since no previous report of arteriography of Castleman tumour in the mesentery could be found, the following case is presented.

CASE REPORT

A 17-year-old female was admitted because of anaemia (haemoglobin 9 g/100 ml), elevated sedimentation rate (90 mm/h) and hypergammaglobulinaemia. The patient had no complaints, and the blood abnormalities were disclosed by a routine school examination. Extensive clinical and radiological examinations did not reveal the cause of the haematological disorder. A palpable abdominal lump was considered to be the lower pole of the right kidney and was checked by palpation during fluoroscopy.

On readmission one year later, after installation of whole body CT-equipment, CT revealed a mass anterior to the right kidney with diameter 45 mm and attenuation value 42 H rising to 57 H following intravenous injection of contrast medium. Review of the aortograms of the previous year disclosed slight stretching of mesenteric arteries and

1981, *British Journal of Radiology*, *54*, 423–425

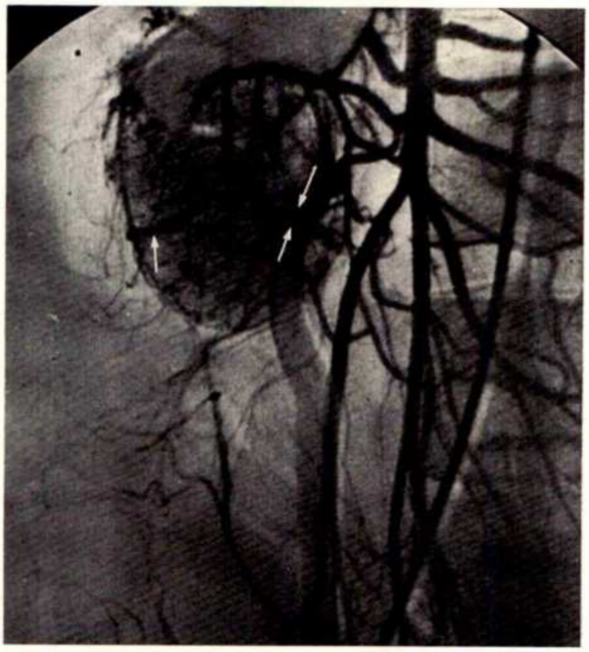


FIG. 1.

Selective arteriography of superior mesenteric artery in patient with mesenteric plasma-cell type Castleman tumour. Highly vascular, round, well -defined mass with early filling of veins (arrows).

prompted a selective arteriography of the superior mesenteric (Fig. 1), right renal and right lumbar arteries. A round, well-defined, richly vascularized tumour was found supplied by branches from the superior mesenteric artery. Early venous filling was present, but there was no prolonged tumour blush. Surgery revealed an encapsulated tumour of the mesentery of the transverse colon, and histological examination showed Castleman tumour of plasma-cell type. Two months after excision of the tumour the abnormal blood laboratory values had returned to normal. No sign of recurrence was found on follow-up examinations, including abdominal CT, 18 months after surgery.

DISCUSSION

In the few previous reports on arteriography of Castleman tumours (Riba, 1979; Tuttle and Shier, 1979; Walter *et al.*, 1978) a richly vascularized mass has been described. In the majority of cases which were of the hyaline-vascular type, a dense, homogeneous blush was present in the capillary phase. The only previous satisfactory description of arteriography of a plasma-cell type of tumour (Riba, 1979), indicated enlarged feeding vessels and venous pooling but no prolonged staining. Similar findings were made in the present plasma-cell type of tumour. Thus the angiographic appearances of the two histological types may differ with regard to prolonged capillary blush. The radiological demonstration of a Castleman tumour is gratifying as surgical excision appears to be curative.

REFERENCES

KELLER, A. R., HOCHHOLZER, L. and CASTLEMAN, B., 1972. Hyalin-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. *Cancer*, *29*, 670–683.

RIBA, P. O., 1979. Castleman's disease. Angiofollicular benign lymph-node hyperplasia. Radiological features in the differential diagnosis of vascular tumours of the pelvis. *British Journal of Radiology*, *52*, 412–414.

TUTTLE, R. J. and SHIER, K. J., 1979. Angiography of angiomatous lymphoid hamartoma (Castleman tumour) and a suggested pathogenesis. *Radiology*, *130*, 311–315.

WALTER, J. F., ROTTENBERG, R. W., CANNON, W. B., SHERIDAN, L. A., PIZZIMENTI, J. and ORR, J. T., 1978. Giant mediastinal lymph node hyperplasia (Castleman's disease): angiographic and clinical features. *American Journal of Roentgenology*, *130*, 447–450.

The anomalous inferior vena cava—another structure between the aorta and the superior mesenteric artery

By *A. Kolbenstvedt, M.D., *F. Kolmannskog, M.D. and †H. H. Lien, M.D.

*Department of Diagnostic Radiology, Rikshospitalet, Oslo 1
†Department of Diagnostic Radiology, The Norwegian Radium Hospital, Montebello, Oslo 3

(*Received November 1980*)

The superior mesenteric artery serves as an important landmark in transverse CT section of the abdomen. The body of the pancreas and the splenic vein arch in front of the artery and may thus be distinguished from the duodenum which traverses the mid-line behind it. The third part of duodenum (Fig. 1A), the uncinate process of the pancreas (Fig. 1A) and the left renal vein (Fig. 1B) have been listed as the three main structures between the superior mesenteric artery and the aorta (Kolbenstvedt *et al.*, 1979).

CASE REPORT

The patient illustrated in the present report (Figs. 2 and 3) was examined with CT of the abdomen because of a malignant tumour of the rectum. No metastases were found, but an unusual structure was situated between the aorta and

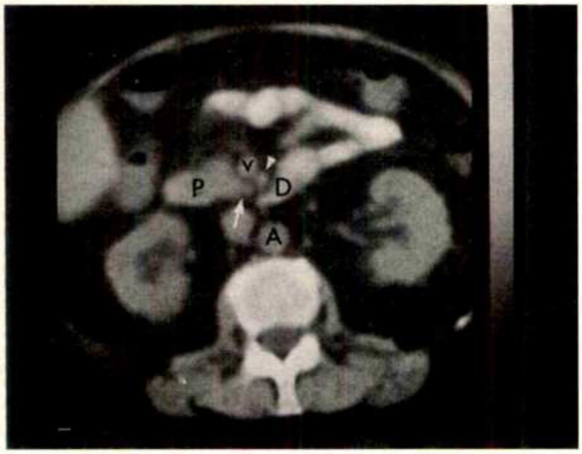


FIG. 1A.

CT section at the level of the lower part of the pancreatic head (P) showing the duodenum (D) and the uncinate process of the pancreas (arrow) between the aorta (A) and the superior mesenteric artery (arrowhead) and vein (V).

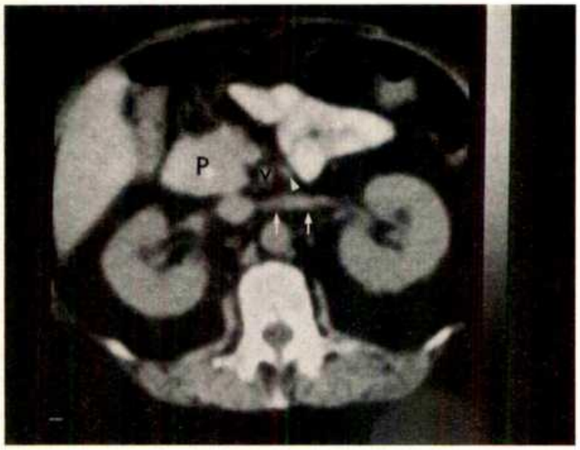


FIG. 1B.

Section at a slightly higher level showing the left renal vein (arrows) between the aorta and the superior mesenteric artery (arrowhead) and vein (V).

the superior mesenteric artery (Fig. 2). At this level the inferior vena cava could not be seen on either side of the aorta, while at lower sections the vein was located to the left of the aorta. Venography confirmed the presence of a left-sided inferior vena cava (Fig. 3) which crossed the midline ventral to the aorta at the level corresponding to that of the left renal vein.

DISCUSSION

A unilateral left-sided inferior vena cava was found in 0.2% of 500 autopsies by Reis and Esenther (1959). Embryologically, the anomaly may be explained as a persistence of the infrarenal segment of the left supracardinal vein.

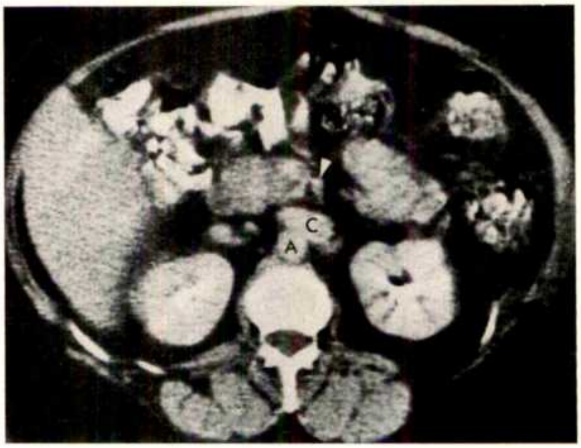


FIG. 2.

CT section showing the inferior vena cava (C) between the aorta (A) and the superior mesenteric artery (arrowhead).

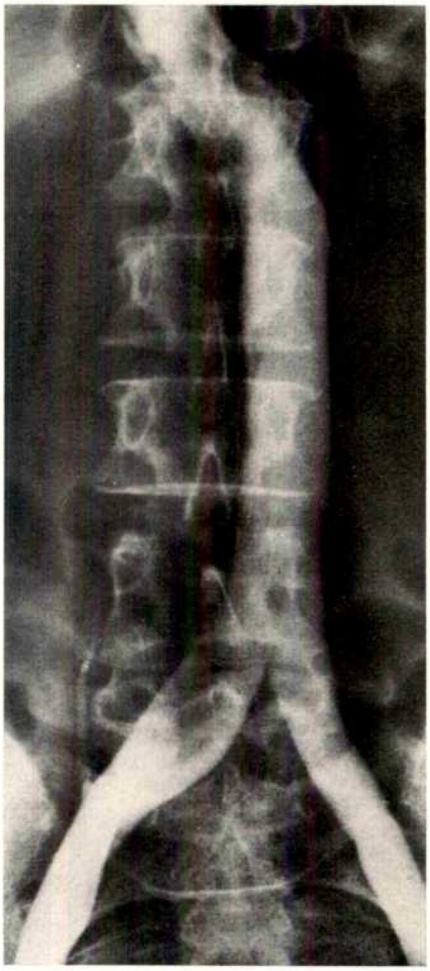


FIG. 3.

Venogram showing a left inferior vena cava which crosses to the right side at the level of the left renal vein.

The anomaly should be considered when a CT section slightly below the body of the pancreas shows an unusual structure between the aorta and the superior mesenteric artery and vein, and the inferior vena cava cannot be traced in its normal position.

REFERENCES

KOLBENSTVEDT, A., KOLMANNSKOG, F. and AAKHUS, T., 1979. Arterial structures of the chest and abdomen at computer tomography. *Acta Radiologica Diagnosis*, *20*, 703–711.

REIS, E. H. and ESENTHER, G., 1959. Variations in the pattern of renal vessels and their relation to the type of posterior vena cava in man. *American Journal of Anatomy*, *104*, 295–318.

Post-biopsy haematuria successfully treated by selective transcatheter epinephrine injection

By Nara Vaeusorn, M.D., Jirakit Viranuvatti, M.D. and Leena Singchoovong, M.D.

Department of Radiology and Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 7, Thailand

(*Received November 1980*)

Transcatheter arterial embolization to control renal haemorrhage is now being used with increasing frequency, particularly in those patients suffering from post-biopsy renal bleeding. An infarct may be an undesirable outcome which may be very important in a patient who already has a poorly functioning or non-functioning kidney. This article describes the successful control of such haemorrhage by transcatheter injection of epinephrine directly into the injured artery. This technique is recommended as an alternative to embolization in patients with impaired renal function or when super selective catheterization of the injured vessel is not possible.

CASE REPORT

A 28-year-old male patient had renal disease and hypertension and was referred to Siriraj Hospital for further investigation. Percutaneous needle biopsy of the right kidney was performed, revealing glomeruli almost completely sclerotic, with diffuse fibrotic interstitial infiltration consistent with end stage renal disease. Thirty minutes after the biopsy the patient experienced severe right-sided abdominal pain. Two hours later massive haematuria developed with the passage of blood clots. Treatment included blood and fluid transfusions, continuous bladder irrigation for removal of blood clots, and administration of diuretics, analgesics and antibiotics. The haematuria gradually subsided and disappeared in two weeks. He was discharged 10 days after the urine and the temperature had returned to normal.

Six days after discharge, massive haematuria with blood clots recurred and he was re-admitted. Bladder irrigation disclosed fresh blood with numerous clots. His haematocrit dropped from 22 to 14.5% within four days. Massive haematuria persisted despite blood transfusion and other supportive and symptomatic therapy. Renal angiography revealed a small area of extravasation of contrast medium from the peripheral dorsal branch of the artery to the upper pole of the right kidney (Fig. 1). A superselective catheterization of the injured arterial branch was performed and 14 μg of epinephrine were slowly injected through the catheter. Twenty minutes later angiography was repeated with the catheter in the main right renal artery. The study showed spasm of the proximal part of the injured arterial branch with an avascular area previously supplied by this artery (Fig. 2). There was no more leakage of the contrast medium. The haematuria improved within a few hours and the urine was clear within twenty-four hours. Some old blood clots were still evacuated upon daily irrigation of the bladder but no fresh haematuria occurred. The patient was discharged 19 days later.

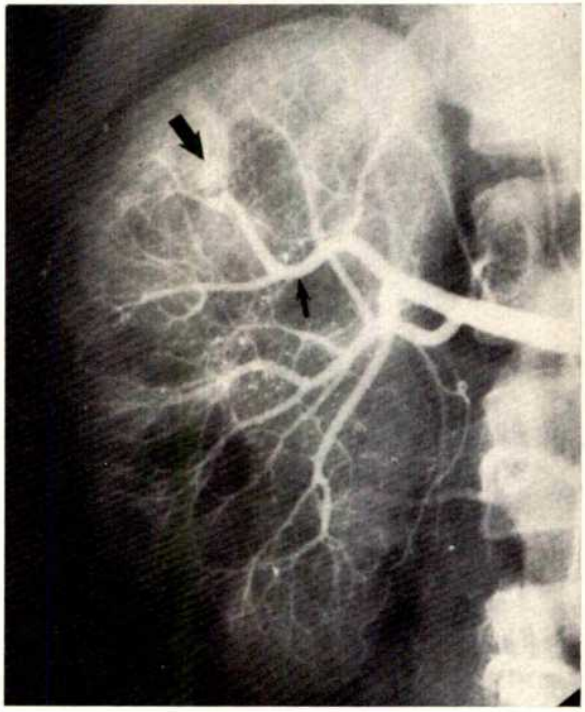


FIG. 1.

Selective right renal arteriography reveals extravasation of contrast medium (big arrow) from the dorsal branch of the artery to the upper pole of the kidney corresponding with the biopsied area. Further advance of the catheter tip to the point indicated by small arrow was subsequently made before epinephrine administration.

Address for reprints: Nara Vaeusorn, M.D., Department of Radiology, Siriraj Hospital, Bangkok 7, Thailand.

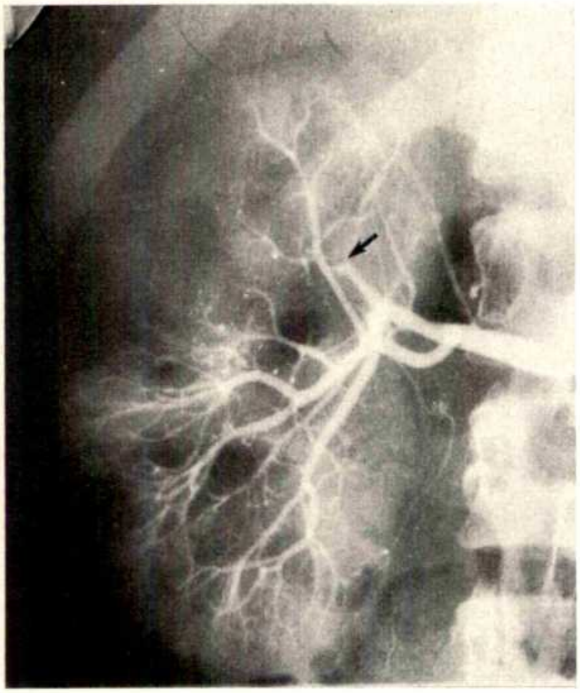


FIG. 2.

Twenty minutes after transcatheter injection of 14 μg epinephrine and the catheter being withdrawn into the main renal artery, the study reveals spasm of the proximal portion of the injured artery (arrow) resulting in an avascular area about the biopsied region.

DISCUSSION

Selective transcatheter embolization to control renal haemorrhage is now widely accepted as a successful alternative to surgery (Chuang *et al.*, 1975; Silber and Clark, 1975; White, 1976; Barbaric and Cutcliff, 1976; Richman *et al.*, 1977). The procedure is not without risk, and the embolized particles can reflux from the catheterized artery and lodge in other vessels, resulting in infarction of neighbouring tissue. This reflux can occur even with gentle injection of embolized particles. Contractile response of the vessel may be induced by the first few injected particles and occlusion of the arterial lumen may occur within few centimetres of the catheter tip. The rest of the injected particles then escape into neighbouring vessels. Bookstein and Goldstein (1973) reported a case of haematuria after renal biopsy controlled by selective arterial embolization when a renal infarct was found at autopsy. The injured artery must therefore be selectively catheterized and only a few pieces of embolized particles should be gently injected at a time. Sometimes the injured artery cannot be catheterized and only a proximal larger artery can be entered: embolization therefore cannot be performed. In this circumstance epinephrine injection is recommended. Furthermore epinephrine should also be employed in a patient who has a poorly functioning or non-functioning kidney, in order to spare as much normal parenchyma as possible. Renal haemorrhage is controlled by contraction of the smooth muscle of the artery by direct action of the epinephrine, and this is followed by clot formation. Another advantage of epinephrine is its similar action on the vein. Study of Olin and Reuter (1965) showed that after injection of 0.20 μg/kg body weight of epinephrine in the renal artery, there were constrictions of the renal artery as well as its branches and also the peripheral venous channels. There was also minimal narrowing of the main renal vein. No change of blood pressure was observed in their fourteen examinations. Other investigators (Smith *et al.*, 1975; Goldman *et al.*, 1978; Pingoud *et al.*, 1979) have used epinephrine injection into the renal artery to enhance renal phlebography with doses from 8–10 μg to 25 μg per single injection, and no undesirable effect was reported.

REFERENCES

BARBARIC, Z. L. and CUTCLIFF, W. B., 1976. Control of renal arterial bleeding after percutaneous biopsy. *Urology*, *8*, 108–111.

BOOKSTEIN, J. J. and GOLDSTEIN, H. M., 1973. Successful management of postbiopsy arteriovenous fistula with selective arterial embolization. *Radiology*, *109*, 535–536.

CHUANG, V. P., REUTER, S. R., WALTER, J., FOLEY, W. D. and BOOKSTEIN, J. J., 1975. Control of renal hemorrhage by selective arterial embolization. *American Journal of Roentgenology*, *125*, 300–306.

GOLDMAN, M. L., GORELKIN, L., RUDE, J. C., SYBERS, R. G., and O'BRIEN, D. P., 1978. Epinephrine renal venography in severe inflammatory disease of the kidney. *Radiology*, *127*, 93–101.

OLIN, T. B. and REUTER, S. R., 1965. A pharmacoangiographic method for improving nephrophlebography. *Radiology*, *85*, 1036–1042.

PINGOUD, E. G., PAIS, S. O. and GLICKMAN, M., 1979. Epinephrine renal venography in acute bacterial infection of the kidney. *American Journal of Roentgenology*, *133*, 665–669.

RICHMAN, S. D., GREEN, W. M., KROLL, R. and CASARELLA, W. J., 1977. Superselective transcatheter embolization of traumatic renal hemorrhage. *American Journal of Roentgenology*, *128*, 843–846.

SILBER, S. J. and CLARK, R. E., 1975. Treatment of massive hemorrhage after renal biopsy with angiographic injection of clot. *New England Journal of Medicine*, *292*, 1387–1388.

SMITH, J. C. JR., RÖSCH, J., ATHANASOULIS, C. A., BAUM, S., WALTMAN, A. C. and GOLDMAN, M., 1975. Renal venography in the evaluation of poorly vascularized neoplasms of the kidney. *American Journal of Roentgenology*, *123*, 552–556.

WHITE, R. I. JR., 1976. Arterial embolization for control of renal hemorrhage. *Journal of Urology*, *115*, 121–122.

1981, *British Journal of Radiology*, *54*, 427

Case reports

Osteopathia striata with sclerosis and thickening of the skull

By M. R. Paling, M.R.C.P., F.R.C.R., I. Hyde, F.R.C.P.(E)., F.R.C.R. and N. R. Dennis, B.A., M.R.C.P.

Departments of Paediatric Radiology and Child Health, Southampton General Hospital

Addendum to paper published in THE BRITISH JOURNAL OF RADIOLOGY, April 1981, *54*, 344–348.

Since this paper was submitted further published cases have come to our attention. Horan and Beighton (1978) describe two families showing clear evidence of autosomal dominant inheritance of osteopathia striata with cranial sclerosis. Whyte and Murphy (1980) describe a family with three cases of osteopathia striata with white forelock and pigmentary skin abnormalities. Franklyn and Wilkinson (1978) describe two cases of osteopathia striata with deafness and cranial osteopetrosis but without sufficient data to assess any genetic contribution.

REFERENCES

FRANKLYN, P. P. and WILKINSON, D., 1978 Two cases of osteopathia striata, deafness, and cranial osteopetrosis. *Annales de Radiologie*, *21*, 91–93.

HORAN, F. T. and BEIGHTON, P. H., 1978. Osteopathia striata with cranial sclerosis. An autosomal dominant entity. *Clinical Genetics*, *13*, 201–206.

WHYTE, M. P. and MURPHY, W. A., 1980. Osteopathia striata associated with familial dermopathy and white forelock. *American Journal of Medical Genetics*, *5*, 227–234.

Book review

Quality Assurance of Radiopharmaceuticals: A guide to hospital practice. Ed. M. Frier and S. R. Hesslewood. 1980. pp. 57. (*Nuclear Medicine Communications*, Special issue) (Chapman & Hall in association with British Nuclear Medicine Society, London). £4·50.
ISBN 0-412-23270
ISSN 0-413-3636

This little paperback was compiled, as we are informed in the foreword, by a group of young radiopharmacologists. It is intended to be a practical guide, for all those involved in the preparation and use of radiopharmaceuticals, to methods used in quality assurance.

In the first ten pages, the general principles underlying nine aspects of product control are identified and briefly discussed under the headings: radionuclide concentration; radionuclide purity and identity; radiochemical purity; chemical purity; sterility; apyrogenicity; absence of foreign matter; measurements of particle size, and pH.

Descriptions of some practical methods that may be used in assay and quality-control procedures follow in the next 16 pages and then three pages are devoted to outlining so-called "process controls": documentation of procedures; record keeping; monitoring of working environment; equipment calibration and operator techniques.

The remaining 20 pages contain monographs on some 30 radiopharmaceutical products, mostly Tc compounds. These are not, as one might have wished, tried, tested and recommended experimental methods for their preparation but rather lists of the various specifications which satisfactory products have to meet. No clues are given as to what to do if a product is found not to meet its specification (throw it away and start again with your fingers crossed?).

At the outset the editors remind us that radiopharmacy is a multidisciplinary subject, so it is a pity that they appear not to have engaged a multidisciplinary team to write this booklet. Those sections concerned with purely physical measurements, for instance, seem rather weak and I was dismayed to read in the section on radioactivity measurements the statement: "in the absence of suitable measuring equipment it may be necessary to determine the activity of a given volume of solution by calculation from the known activity concentration of the bulk material."

Surely in such a publication as this it is irresponsible to condone such a practice which, for a variety of reasons, can give rise to considerable errors. No pharmacy can do without a balance and no radiopharmacy can do without equipment for measuring activity. If a dedicated instrument is not available (as it should be), even a gamma-camera can be calibrated and pressed into service for this purpose if necessary!

The paragraphs on methods of determining aspects of chemical and radiochemical purity are far better but could have been improved by the inclusion of references to other sources of more detailed information. Indeed, the lack of references is noticeable throughout the book.

With both the BIR and the HPA having previously published booklets* giving guidance on the preparation of radiopharmaceuticals in hospitals, it was perhaps inevitable that the BNMS, the third British organization with a professional interest in this subject, should sponsor its own publication, and it is certainly inevitable that it will be judged by comparison with its predecessors despite the fact that its aims and content are more limited.

Unfortunately, being produced from "camera-ready typescript" it compares very unfavourably in style and presentation. Its scientific content forms a useful adjunct to the earlier works at a price all should afford, but the definitive radiopharmaceutical laboratory handbook still remains to be written.

D. J. SILVESTER.

---

*British Institute of Radiology. 1975 (revised 1979). Guidance for the preparation of radiopharmaceuticals in hospitals. BIR Special Report 11.
Hospital Physicists Association. 1977. The hospital preparation of radiopharmaceuticals HPA Scientific Report Series 16.

1981, *British Journal of Radiology*, 54, 428

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

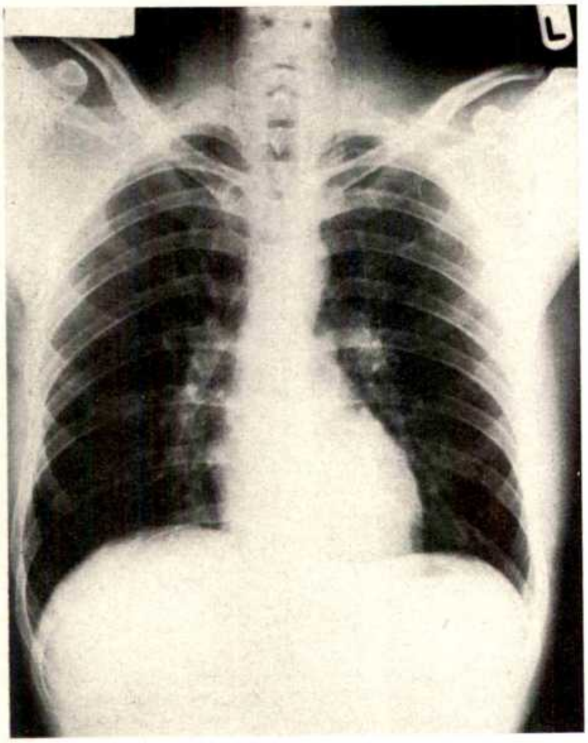


FIG. 1.

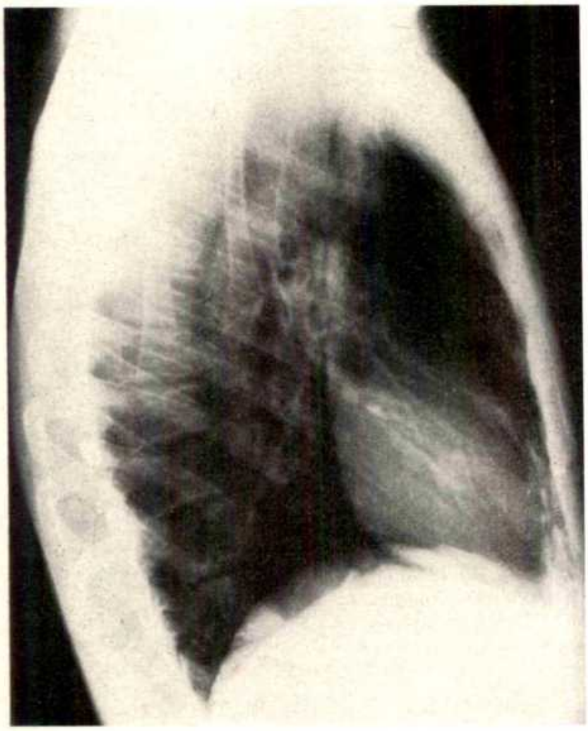


FIG. 2.

Occult pneumothorax

THE EDITOR—SIR,

The diagnosis of pneumothorax is usually a simple matter. PA films in expiration usually show it and a horizontal beam lateral has been recommended particularly in children.

Recently a 24-year old patient came to this hospital with a history of eight hours' chest pain. Clinical diagnosis of pericarditis was made and the patient referred for a chest X-ray. On the PA film no abnormality was detected (Fig. 1). However, on the lateral the lung edge could be seen just behind the sternum (Fig. 2). On the basis of this the diagnosis changed to pneumothorax. Over a period of ten days the lateral chest film reverted to normal and the patient's symptoms resolved.

I wonder if anybody else has found the lateral view valuable in such cases?

Yours, etc.,
A. COHEN.

Department of Radiology,
Royal Hospital,
Chesterfield S41 7SP.
(*Received December 1980/February 1981*)

A cautionary note on the use of thiol compounds to protect normal tissues in radiotherapy

THE EDITOR—SIR,

The demonstration by Yuhas of selective radioprotection of normal tissues over tumours with the thiophosphate compound WR2721 (Yuhas and Storer, 1969) aroused considerable interest in the use of this and related thiol compounds in clinical radiotherapy. Subsequent investigations indicated that there was a lower uptake of WR2721 by tumours than by normal tissues (Yuhas *et al.*, 1977), which increased hopes that use of the drug might give a substantial therapeutic gain. However, other investigations (Phillips *et al.*, 1973; Rojas and Stewart, 1980) have failed to substantiate the very low protective effect on tumours by WR2721 reported by Yuhas and have shown a wider variation in the protection afforded to normal tissues than was previously reported. These discrepancies suggest that considerable caution should be adopted and that further studies are required to provide an understanding of the conditions in which thiol compounds might protect, or fail to protect, tumours relative to normal tissues.

WR2721 has to be dephosphorylated to a free thiol compound before it can act as a radioprotective agent (Harris and Phillips, 1971). Studies in our laboratories of the influence of thiol compounds on the radiobiological oxygen effect are therefore of some relevance. Cullen *et al.* (1980) have shown that when free thiol levels in cells are increased the degree of radioprotection achieved varies with the concentration of oxygen in the cell suspension. The degree of protection is least either in air of in oxygen-free nitrogen (<10 p.p.m.) and is maximal at an intermediate oxygen concentration which is about equal to the radiobiological oxygen effect K-value for the cells (Fig. 1). Thus, partially hypoxic cells, widely considered to be present in tumours, are more readily protected by an $-$SH compound than are well oxygenated cells. Consequently, although the poor vascularity of tumours, or other factors associated with transport into cells, may result in a lower concentration of radioprotective compound in tumour cells than is achieved in the normal tissue, that reduced level of radioprotector may still produce as great or even greater a protective effect on the partially hypoxic tumour fraction as is obtained in the normal tissue. Such protection could result in regrowth of the tumour. Therefore there are likely to be circumstances in which the use of compounds such as WR2721 may be a

1981, *British Journal of Radiology*, *54*, 429–430

Correspondence

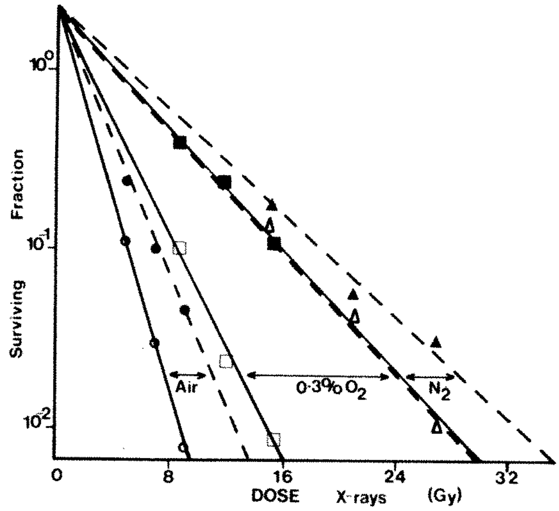


FIG. 1.

Survival curves of exponentially growing mouse Ehrlich Landschutz tumour cells irradiated in three different oxygen concentrations with and without 10 mM dithioerythritol (DTE) ○ Air; ● Air+DTE; □ 0·3% O_2; ■ 0.3% O_2+DTE; △ N_2; ▲ N_2+DTE.

positive disadvantage in radiotherapy. The extent to which a larger protective effect will be obtained in the tumour than in the normal tissue will depend on the degree of hypoxic protection in the tumour, which is known to vary considerably among experimental tumours. It would be useful to investigate whether some degree of correlation exists between the therapeutic gain with a thiol compound and the extent of hypoxic protection in a tumour. Clearly if such a correlation does exist any clinical application would require some knowledge of the variation in degree of hypoxia among types of human tumour.

Yours, etc.,

J. LUNEC,
BEULAH CULLEN,
HILARY WALKER,
SHIRLEY HORNSEY.

MRC Cyclotron Unit,
Hammersmith Hospital,
London W12 0HS.

(*Received February 1981*)

REFERENCES

CULLEN, B. M., MICHALOWSKI, A., WALKER, H. C. and RÉVÈSZ, L., 1980. Correlation between the radiobiological oxygen constant, K, and the non-protein sulphydryl content of mammalian cells. *International Journal of Radiation Biology*, *38*, 525–535.

HARRIS, J. W. and PHILLIPS, T. L., 1971. Radiobiological and biochemical studies of thiophosphate radioprotective compounds related to cysteamine. *Radiation Research*, *46*, 362–379.

PHILLIPS, T. L., KANE, L. and UTLEY, J. F., 1973. Radioprotection of tumour and normal tissues by thiophosphate compounds. *Cancer*, *32*, 528–535.

ROJAS, A. M., and STEWART, F., 1980. Radioprotection by WR2721 in normal mouse skin and tumour. British Institute of Radiology: Radiobiology Work-in-Progress Meeting: Radiosensitizers and Radioprotectors, Nov. 21, 1980 (Abstracts to appear in *British Journal of Radiology*, *54*, 1981).

YUHAS, J. M., and STORER, J. B., 1969. Differential chemoprotection of normal and malignant tissues. *Journal of the National Cancer Institute*, *42*, 331–335.

YUHAS, J. M., YURCONIC, M., KLIGERMAN, M. M., WEST, G., and PETERSON, D. F., 1977. Combined use of radioprotective and radiosensitising drugs in experimental radiotherapy. *Radiation Research*, *70*, 433–443.

A comparison between two hysterosalpingographic contrast media—Urografin 370 and Isteropac

THE EDITOR—SIR,

Contrast media used in hysterosalpingography should possess sufficient viscosity to limit leakage back into the vagina and for the contrast medium to remain in the uterine cavity and the fallopian tubes long enough for their radiographic demonstration. The viscosity of some contrast media, such as Urografin 370, depends on their high concentration. Other hysterosalpingographic contrast media contain additives which act as "stiffeners" to increase their viscosity. Isteropac consists of two viscous additives, propylene glycol and sodium carboxymethylcellulose, together with the water soluble contrast agent iodamide.

We have recently compared the properties of Urografin 370 and Isteropac in regard to their ease of injection, complication rate and radiographic qualities. The study consisted of 100 consecutive patients with primary infertility who were referred for hysterosalpingography, 50 receiving Urografin 370 while Isteropac was used in the other 50 patients by random allocation. The identity of the contrast medium was withheld from the clinical assessor, the gynaecologist who performed the investigations and from the radiologist who assessed the hysterosalpingograms. A standard cannulation and injection technique was used throughout the study.

Pain at various stages in the investigation was graded as 0 (absent), 1 (slight), 2 (moderate) and 3 (severe). While there was no significant difference between the two groups regarding the incidence and severity of pain at the time of instrumentation (χ^2=1.749, P=0.63) (Table I), Isteropac caused more pain on injection than Urografin 270 (χ^2=10.619, P=0.014). Pain on peritoneal spill was also greater with Isteropac than with Urografin 370 (χ^2=11.231, P=0.011), but no significant difference in pain developing within the next two hours was apparent (χ^2=2.333, P=051). There was no significant difference between the ease of injection of Isteropac and Urografin 370 (χ^2=1.555, P=0.56), or in the degree of leakage into the vagina (χ^2=1.258, P=0.73). Both Urografin 370 and Isteropac were regarded as providing good contrast density and showed no significant difference in respect to the density of uterine opacification, delineation of the cervix and uterine body, delineation of the fallopian tubes and ease of peritoneal spill and spread.

TABLE I

INCIDENCE OF PAIN WITH BOTH CONTRAST MEDIA

	Isteropac				Urografin 370			
	0	1	2	3	0	1	2	3
Pain due to instrumentation	2	27	18	3	3	31	15	1
Pain due to injection of contrast medium	1	7	28	14	3	20	19	8
Pain with peritoneal spill	1	7	21	17	7	14	18	4
Delayed pain	34	9	7	0	34	9	5	2

Reiss and Grossman (1958), and McNabb (1959) have found Urografin 370 to be a satisfactory hysterosalpingographic contrast medium. Two Italian series (Samaden and Baici, 1972; Tetti *et al.*, 1972) have found Isteropac to be a satisfactory contrast agent which is well tolerated and associated with only a low incidence of pain. A single report some years ago (Bergman *et al.*, 1953) stated that carboxymethylcellulose, when used as a viscogenic agent in combination with water soluble contrast media for hysterosalpingography, was found to stimulate foreign body granulomas in the myometrium and fallopian tubes and on the ovaries. In conclusion, Urografin 370 is prefered to Isteropac on the basis of the possibility of granuloma formation and the higher incidence of pain with the latter agent.

Yours etc.,
G. H. WHITEHOUSE,
C. SAUSMAN.

X-ray Department
Women's Hospital,
Catherine Street,
Liverpool L8 7NJ.
(*Received February 1981*)

REFERENCES

BERGMAN, F., GORTON, G., NORMAN, O. and SJOSTEDT, S., 1953. Foreign body granulomas following hysterosalpingography with a contrast medium containing carboxymethylcellulose. *Acta Radiologica*, *43*, 17–29.

MCNABB, R. W., 1959. The technique and use of Urografin as a contrast medium in hysterosalpingography. *Radiologists*, *10*, 108–110.

REISS, H. E. and GROSSMAN, M., 1958. Experience with new contrast media for hysterosalpingography. *Journal of Obstetrics and Gynaecology of the British Empire*, *65*, 782–787.

SAMADEN, R. and BAICI, R. F., 1972. Evaluation of a new water-soluble contrast medium for hysterosalpingography. *Minerva Ginecologica*, *24*, 61–72

TETTI, A., DAVITTI, L. and PAZZAGLIA, L., 1972. The diagnostic possibilities of a new viscous and water soluble contrast medium for hysterosalpingography. *Radiologica Medica*, *58*, 707–715.

The use of diagnostic ultrasound to measure the lumbar spinal canal

THE EDITOR—SIR,

A recent letter to this journal (Stockdale and Finlay, 1980) expressed serious doubts about the validity of the use of ultrasound for the measurement of the lumbar spinal canal. We have recently carried out a detailed scientific investigation into the interaction of ultrasound with the internal structures of the spine in an attempt to confirm or refute the technique on scientific grounds. Our full work will be published shortly, but in the light of our findings we would like to comment on some of the points raised by Stockdale and Finlay.

Before attempting to apply any new technique to clinical diagnosis one must first develop a practical protocol based upon rigorous scientific analysis. Our investigations were in three parts, first to establish the origin of the echoes observed in practice, second to establish formal criteria according to which these echoes may be detected and optimized, and finally to determine a method for their measurement yielding the greatest realistic degree of accuracy and reproducibility.

Our findings were that by linearly scanning in a longitudinal plane inclined at 15° to the sagittal plane one can obtain B scan images, with identifiable A-scan peaks, representing an oblique sagittal dimension of the spinal canal. At this angle, the greatest proportion of the ultrasonic energy is traversing the central region of the canal and the dimension measured is most likely to reflect changes in its cross-sectional shape. Furthermore, at this angle the lateral displacement of the transducer may be uniquely defined for a given vertebra, according to criteria which yield the best echo differentiation from the noise level for echoes of equal amplitude.

We agree with Stockdale and Finlay that different dimensions can be measured corresponding to different orientations across the canal space, according to the angle of inclination to the sagittal plane and the lateral displacement of the transducer. For this reason it is essential that a fixed scanning angle is adopted and criteria established to define the lateral displacement uniquely for any given vertebra. Having done this, the separation of the principal echoes may be measured to a high degree of accuracy using electronic measuring facilities on the A-scan display.

Certainly the potential error in a single measurement of the spinal canal is large. Consequently the scanning protocol must be designed in such a way as to standardize as many of the variables as possible. Repeated measurements should be made at each vertebral level, and only their mean value accepted. These measures will diminish the effects of random error, such as spinal rotation, etc., and reduce the probable error to an acceptably low level. It is this probable error which is representative of the degree of reproducibility obtainable in practice.

We have achieved a reproducibility of 0.1 mm in carefully controlled *in vitro* experiments, which greatly exceeds that claimed by Porter *et al.* (1978). *In vivo* measurements have achieved a reproducibility of approximately 0.4 mm under clinical conditions.

Stockdale and Finlay did not indicate the degree of sophistication to which their scanning technique had been developed before their *in vivo* measurements were made. Their remarks regarding the difficulty they experienced in recording reliable *in vitro* measurements would imply some uncertainty in their scanning protocol. To attempt the differentiation of symptomatic patients from the normal without a closely defined and tested protocol is courting failure.

We welcome constructive criticism, since this is essential to the proper care and well-being of the patient. However, it would be most regrettable if a new technique were to be cast into disrepute as a result of a superficial survey. We hope this controversy will stimulate other centres into properly controlled investigations. It is essential that each centre should adopt and rigidly adhere to its own scanning technique, established according to accepted scientific criteria. It must establish its own set of normal values for the measurement of each vertebral level. Only when the limits of the normal ranges have been established with proper statistical rigour can any scientific significance be attached to abnormal values.

We believe that under these circumstances the technique is potentially capable of making a valuable contribution to clinical diagnosis.

Yours, etc.
D. OTTEWELL,
P. HOWELLS.

Departments of Medical Physics
and Bioengineering,
Royal Infirmary,
Doncaster DN2 5LT.
(*Received January 1981*)

REFERENCES

STOCKDALE, H. R. and FINLAY, D., 1980. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *53*, 1101–1102.

PORTER, R. W., WICKS, M. and OTTEWELL, D., 1978. Measurement of the spinal canal by diagnostic ultrasound. *Journal of Bone and Joint Surgery*, *60B*, 481–484.

1981, *British Journal of Radiology*, *54*, 431–435 MAY 1981

Proceedings of The British Institute of Radiology

Dosimetry and risks to patients in radiopharmaceutical investigations

Abstracts of papers presented at a meeting held at The British Institute of Radiology on November 26, 1980

Chairmen: Professors B. Nosslin and F. W. Spiers and Drs J. Vennart and N. Veall

Antecedents and scope of ICRU 32: "Methods of assessment and absorbed dose in clinical use of radionuclides", by N. G. Trott.
The need for more metabolic data for the updating of ICRP 17, by B. Nosslin.
Of mice, men and models: data required for dose calculations, by P. Tothill.
Fetal radiation dose from radionuclide venography and lung scan, by L. A. Malone, J. T. Ennis and J. F. Malone.
Dosimetry of renal pharmaceuticals: the importance of bladder radioactivity and a simple aid for its estimation, by T. Smith.
Bone-marrow dose from surface-seeking radionuclides in human bone, by F. W. Spiers.
Estimation of age-dependent absorbed doses from radiopharmaceuticals, by K. Henrichs, A. Kaul and H. D. Roedler.
Basic concepts in ICRP publications 26 and 30, by J. Vennart.
The value of human life, by G. H. Mooney.
ARSAC and the current legal situation in the UK by N. Veall (*no abstract received*).
The ten-day principle and radiopharmaceutical investigations, by D. M. Taylor.
How dangerous is "dangerous"? by M. V. Merrick.
Radiopharmaceutical risks: a view of the pros and cons, by D. H. Keeling.

ANTECEDENTS AND SCOPE OF ICRU 32: "METHODS OF ASSESSMENT OF ABSORBED DOSE IN CLINICAL USE OF RADIONUCLIDES"

By N. G. Trott

Institute of Cancer Research and Royal Marsden Hospital, Downs Road, Sutton, Surrey

The ICRU Report No. 32, published in November 1979, provides, in a single volume of 60 pages, a guide to the principles of radionuclide dosimetry and their applications in clinical work. This report, first conceived in 1961, was prepared during the 1970's, a period of rapid development in the scope of nuclear medicine, in the presentation of data on the properties of radionuclides and the absorption of the radiations they emit, and in the formalism used in evaluating absorbed dose. In this paper an outline was first given of these developments, with particular reference to the work of the Medical Internal Radiation Dose Committee (MIRD) of the United States Society of Nuclear Medicine. It was then explained that ICRU Report 32, which recommends use of the formalism introduced by Loevinger and Berman in 1968, deals with both the physical and the biological aspects of dosimetry. The contents of five appendices to the report were then outlined. It was explained that these provide a considerable range of simplified data on the radiations emitted by many radionuclides of clinical interest and on absorbed fractions for these radiations, give examples of the evaluation of dose for several different types of radiopharmaceutical and include a review of some problems in the dosimetry of the radionuclides ^{3}H, ^{14}C and ^{125}I.

THE NEED FOR MORE METABOLIC DATA FOR THE UPDATING OF ICRP 17

By B. Nosslin

General Hospital, Malmö, Sweden

ICRP Publication 17 deals with protection of the patient in radionuclide investigations. It was published in 1971, and in 1978 ICRP asked a task group to prepare a new report, which should include the new radiopharmaceuticals which have come into use since 1971. For each substance a best estimate of its biokinetics should be given, together with calculated values of absorbed dose for adults (including the range of variation in pathological states), children and the fetus. The task group hopes to deliver its report in 1981.

Published data on biokinetics are scarce, especially with regard to quantitative measurements in man. The clinician is often interested mainly in the initial distribution and metabolism of the substance, while for dosimetry purpose long-term retention is of great interest. The task group wants to encourage people to carry out appropriate measurements, particularly whole-body retention and excretion rates. The results should be expressed as fractions of administered activity, and they should either be published or made available to the task group. Measurements in patients in different conditions are desirable. All opportunities to study uptake in fetus and excretion in milk should also be utilised.

OF MICE, MEN AND MODELS: DATA REQUIRED FOR DOSE CALCULATIONS

By P. Tothill

Department of Medical Physics, The Royal Infirmary, Edinburgh

Mice (and other experimental animals) may be useful in predicting the biological behaviour of radiopharmaceuticals administered to man. Models, consisting of the set of assumed conditions, spatial, structural and kinetic, are essential for dose calculations.

The physical data required, relating to the radionuclides used, are generally accurately known and well documented. Absorbed fractions for most organs as source and target, for a wide range of energies, have been tabulated, but only for a computer model based on Reference Man (though with some hermaphrodite characteristics). For missing organs and subjects of appreciably different size, cruder approximations to absorbed fractions may be necessary.

The biggest uncertainties in data relate to biological factors of the concentration of radioactivity in organs and its variation with time. These factors determine the cumulated activity in various parts of the body. Animal experiments may be used, but the possibility of species differences must be considered. Ultimately, measurements in humans are necessary, and may include whole-body counting, profile scanning, quantitative scintigraphy, blood sampling and uptake counter measurements.

As an example, the steps necessary to obtain dose estimates in various organs for a new radiopharmaceutical, a bile salt analogue labelled with ^{75}Se, were outlined.

FETAL RADIATION DOSE FROM RADIONUCLIDE VENOGRAPHY AND LUNG SCAN

By L. A. Malone and J. T. Ennis

Department of Radiology, Mater Hospital, Dublin

and

J. F. Malone

College of Technology, Kevin Street, Dublin

Radiation doses to the fetus have been estimated for pregnant patients undergoing radioisotope venography using ^{99}Tc^{m}-labelled MAA. Data on the fate of the administered pharmaceutical were obtained from non-pregnant patients having routine lung scans and venograms. This kinetic information was used to calculate the accumulated activity in the organs involved in uptake and elimination of the radioisotope. Since a fetus would be subjected to radiation from these organs, a pregnant-woman phantom was constructed in which doses from known cumulated activities within the maternal organs could be measured within uteri of 3, 6 and 9 month's gestation.

There is obviously a possibility that radioactivity could pass the placental barrier and localize within a fetus. To assess this risk, pregnant rabbits were used to investigate fetal activities and, further, fetal thyroids were assayed since the thyroid was considered to be the most likely target organ.

Adding together the internal and external radiation doses to the fetus, we proceeded to compare the results with those for X-ray contrast venography measured in the same phantom. Skin measurements on patients undergoing both types of venography were compared with those on the phantom and corresponded well.

MIRD tables were used to calculate doses to maternal and fetal organs from our own measurements of cumulated activity. In isotope venography the whole maternal body is irradiated unevenly and so also is the body of the fetus. We, therefore, followed the system of weighting factors set out in ICRP 26 but assigned a total weighting factor of 1 to the mother and a separate total of 1 to the fetus to find the dose equivalent of the method. To compare the result to that for contrast venography we need to account for the fact that here the mother's body is only partly exposed, whereas the whole fetus is irradiated.

The results of our investigations have so far revealed that the dose to the fetus from radioisotope venography is significantly lower than that from contrast venography even allowing for approximately 1% of the administered dose passing the placenta and up to 0.02% being localized in the fetal thyroid in the third trimester. There were some differences between the kinetic data for humans and those for rabbits, the most notable of these being high stomach uptake in humans and low uptake in rabbits. However, the rabbit fetal activities would still supply a good estimate of activity passing the placenta. The dose equivalents were approximately 2 mSv (0.2 rem) for mother and 1 mSv (0.1 rem) for fetus or 3 mSv (0.3 rem) for isotope venography of a pregnant woman using an injection of 190 MBq (5 mCi) ^{99}Tc^{m} MAA. These results will be assessed in the light of the recently published BEIR (Biological Effects of Ionizing Radiations) Committee report, should this be available soon.

DOSIMETRY OF RENAL RADIOPHARMACEUTICALS: THE IMPORTANCE OF BLADDER RADIOACTIVITY AND A SIMPLE AID FOR ITS ESTIMATION

By T. Smith

Northwick Park Hospital, Harrow, Middlesex

The contribution from radioactivity in bladder contents to dose commitments to the embryo, ovaries, marrow, bladder wall and whole body has been estimated for various renal radiopharmaceuticals, assuming a bladder voiding period of three hours. For Hippuran and GFR agents this contribution is 70–75% of the embryo dose and 50–90% of the ovary dose. The embryo dose exceeds the ovary dose by a factor of two or more. For the radiopharmaceuticals with no significant kidney retention, the bladder-wall dose is higher, by more than an order of magnitude, than doses to other organs and is largely responsible for the effective dose equivalent exceeding the estimated whole-body dose by factors of up to 27.

Since the estimation of cumulated activity in bladder contents is necessary for bladder dosimetry, a nomogram, based on a three hour voiding period, is proposed as a convenient aid for this purpose.

BONE-MARROW DOSE FROM SURFACE-SEEKING RADIONUCLIDES IN HUMAN BONE

By F. W. Spiers

Bone Dosimetry Research Unit, The University of Leeds, Cookridge Hospital, Leeds LS16 6QB

Based on calculations by Spiers *et al.* (1978; 1981), a comparison is made between the dose to bone marrow from bone volume-seeking and bone surface-seeking β-particle emitters. Results are given for human bone for three ages, 1.7, 9 and 44 years and for radionuclides covering a mean β-particle energy range from 0.0255 MeV to 0.927 MeV. These show that at low energies, *e.g.* 0.05 MeV, the bone marrow dose from a surface-seeking radionuclide is an order of magnitude greater than from a volume-seeker. At high β-particle energies, *e.g.* 1 MeV, the ratio of the doses is more than two.

The results may have clinical significance because some radionuclides spend an appreciable time on bone surfaces before being finally distributed throughout the bone volume. Only limited metabolic data of this kind are at present available but data have been reported on the metabolism of the alkaline earth elements in man by a task group of the International Commission on Radiological Protection (1972). Combining these data with the dosimetry calculations it is shown that, in the case of ^{45}Ca, the dose calculation that includes both the surface and the volume depositions gives integrated doses to ten days and 100 days after injection that are respectively 4.5 and 1.9 times the corresponding values calculated conventionally on a volume deposition only. Other radionuclides considered in this way are ^{47}Ca (ratio 2.4 to 2.1 times the conventional figure) and the two strontium isotopes ^{89}Sr and ^{90}Sr, for which the ratios are only significantly greater than unity for integration times of less than about 50 days.

REFERENCES

International Commission on Radiological Protection, 1972. Alkaline Earth Metabolism in Adult Man. ICRP Publication No 20, (Pergamon Press, Oxford).

Spiers, F. W., Beddoe, A. H. and Whitwell, J. R., 1978. Mean skeletal dose factors for beta-particle emitters in

human bone. Part I. Volume-seeking radionuclides. *British Journal of Radiology*, *51*, 622–627.
1981. Part II. Surface-seeking radionuclides. *British Journal of Radiology*, *54*, (in press).

ESTIMATION OF AGE-DEPENDENT ABSORBED DOSES FROM RADIOPHARMACEUTICALS

By K. Henrichs and A. Kaul

Free University Berlin, Klinikum Steglitz,
Hindenburgdamm 30, D-1000 Berlin 45

and H. D. Roedler

Federal Health Office,
Ingolstaedter Landstr., D-8042 Neuherberg, Germany

The radiation dose absorbed in a target organ or the total body depends on both the dose absorbed in the target per disintegration (specific absorbed dose) and the number of distintegrations in a source organ (cumulated activity). Both quantities depend on the patient's age: the specific absorbed dose mainly depends on the mass, size and shape of the organs and on their mutual distance; the cumulated activity depends on the metabolic behaviour of the radiopharmaceutical in the organism, *e.g.* gastrointestinal resorption, inhalation rates, turnover rates or mean residence times.

Values of the specific absorbed dose for 62 radionuclides were used, and on this basis the effective whole-body dose equivalents for 28 radiopharmaceuticals were calculated, as a function of age, by modifying the existing values for the adult reference man depending on the type of radiation (non-penetrating and penetrating radiation) emitted by the radionuclide, on the organ mass, and on the mutual distance of the source-target pairs (calculated by a reduction of target and source volumes to their centres of mass and shrinkage of their co-ordinates according to the age-dependent dimensions of the trunk).

This approximate method, however, is only applicable to those source–target pairs for which the definition of centres of mass is justified; this does not prove true for skeleton, skin and bone marrow. For these targets the maximal over-estimate of specific absorbed doses by the approximate method amounts to a factor of four (source = liver, target = active bone marrow) as compared to results of Monte-Carlo calculations using age-dependent mathematical phantoms and the distribution of the active bone marrow as a function of age.

The results of a literature search on age-dependent biokinetic data as a prerequisite for calculating the cumulated activities can be summarized as follows:

only few (less than 4%) of the publications reviewed contain biokinetic data suitable for dosimetric purposes;

for the radiopharmaceuticals labelled with short-lived radionuclides such as $^{99}Tc^{m}$ and ^{123}I, generally recommended for administration to children, variations of the biological halftimes with age may be neglected. Therefore for the paediatric application of radiopharmaceuticals the absorbed dose can be calculated based upon the biological half-times of the adult;

hardly any information is available on the age-dependence of the fractional uptake of radioactive substances from the transfer-compartment to any organ.

Only in the case of radio-iodide are sufficient biokinetic data known from the literature.

In conclusion, it may be stated that the mathematical models at present used for the modification of values of specific absorbed doses in the adult, considering age-dependent changes of mass and localization of the organs, prove to be of sufficient accuracy: in comparison to the few available values calculated by Monte-Carlo techniques this method overestimates the specific absorbed fractions by a factor of four for the worst case (target = active bone marrow; age-dependent distribution). For practical radionuclide dose-estimates, these deviations are of minor importance as long as reliable information is lacking on the metabolic behaviour of radionuclides as a function of age (*e.g.* with regard to the gastro-intestinal resorption, the uncertainty can amount to a factor of 100).

This proves true also for radiopharmaceutical dosimetry as far as there is only incomplete information on organ uptake values. The uncertainty of the biological half-times and gastro-intestinal resorption, however, is of little importance considering both the short-lived radionuclides and the routes of administration which are mainly used in paediatric nuclear medicine.

BASIC CONCEPTS IN ICRP PUBLICATIONS 26 AND 30

By J. Vennart

MRC Radiobiology Unit, Harwell, Oxon

The recommendations of ICRP in Publication 26 differ from all its previous recommendations by being quantitatively based on a relationship between risk and dose. Two types of effect are considered. Stochastic effects are those for which the probability of an effect occurring, rather than its severity, is regarded as a function of dose without threshold; the most important are cancer in irradiated individuals and serious hereditary disease in their descendants. Non-stochastic effects are those for which the severity varies with the dose and for which a threshold may therefore occur, such as cataract and loss of fertility.

The recommended dose limits are now only part of a wider system that requires justification of the use of sources of ionizing radiation and optimization so that all doses are kept as low as reasonably achievable. In medical exposure, doses should be limited to the minimum consistent with the medical benefit to the individual patient. For workers and members of the public the limits for stochastic effects are based on a comparison of the risks of radiation-induced fatal cancer and serious hereditary disease with those of fatalities in other industries and in everyday life respectively. ICRP then confirms the previous recommended limits for uniform irradiation of the body of 0.05 Sv (5 rem) for a worker and 5 mSv (0.5 rem) for a member of the public in any year of practice. However, adequate justification would be required for any plan that included long continued exposure of a considerable fraction of workers at or near the dose limit and for long-continuing exposure of a member of the public the dose should be limited to 1 mSv (0.1 rem) per year.

Non-uniform irradiation of the body is limited so that the total risk of stochastic effects in all the tissues irradiated is no greater than that from the appropriate limit on uniform whole-body irradiation. There are additional constraints to prevent non-stochastic effects, namely annual limits on dose for a worker of 0.15 Sv (15 rem) in the lens and 0.5 Sv (50 rem) to any other tissue and for a member of the public of 0.05 Sv (5 rem) in any tissue. Annual limits on the intake of radioactive materials, the ALIs, are derived so that the resulting doses to all tissues over the succeeding 50 years do not exceed the annual limits on dose recommended by the Commission.

Limits for intakes of radionuclides are discussed in ICRP Publication 30 of which Parts 1 and 2 have been published and the final Part 3 will be published shortly. Part 1 describes the methods of calculation and the basic dosimetric models. Then follow data on the metabolism of chemical compounds of each element and a table of ALIs and Derived Air Concentrations (DACs) for each of its radioisotopes with radioactive half-periods greater than ten minutes. Tables of the computer output used to calculate ALIs and DACs are given in a supplement to each part and data on the radioactive decay schemes used will be the subject of a separate publication.

THE VALUE OF HUMAN LIFE

By G. H. Mooney

Health Economics Research Unit, University of Aberdeen

It is possible in economic terms to see the ICRP's concept of "detriment" as the equivalent of one aspect of social cost in the economic calculus of (social) cost- (social) benefit analysis. The major difficulty in using cost-benefit analysis lies in valuing all benefits and all costs on the common measuring rod of money. This was exemplified in the context of valuing human life, which can be achieved, depending on the underlying value judgments made, on the basis of one of three different approaches—the present value of lost output, willingness to pay on the part of potential victims to reduce the risk of death, or considering the values already implicit in existing decision making. The last approach was described using the example of mammography in breast cancer screening. In conclusion it was emphasized that it is not possible to avoid valuing life.

THE TEN-DAY PRINCIPLE AND RADIOPHARMACEUTICAL INVESTIGATIONS

By D. M. Taylor

Lehrstuhl für Strahlentoxikologie der
Universität Heidelberg, In Neuenheimer Feld 345,
D-6900 Heidelberg, Federal Republic of Germany

The applicability of the ten-day principle in nuclear medicine is a matter of controversy. Ellis and other members of the former MRC Isotope Advisory Panel recommended that the principle should apply to all investigations where the gonad radiation dose would exceed 0.5 mSv (50 mrem), unless the effective half-life of the radiopharmaceutical is long compared to ten days (Ellis *et al.*, 1977). This view has been strongly criticized and others have suggested a limit of 5 mSv (Sear, 1978; Taylor, 1979; Nuclear Medicine Communications, 1980) which would exclude the majority of nuclear medicine procedures from the application of the rule.

Is the gonad dose the correct parameter for decision? How "safe" is a limit of 5 mSv? These are important questions. The dose to a possible embryo may be the more appropriate parameter, especially since recent calculations (Husak and Wiedermann, 1980) suggest that the ratio embryo: gonad dose lies in the range 0.75 to 1.9 for many common radiopharmaceuticals. The additional risk of severe malformation or cancer arising in an offspring has been calculated to be about 5×10^{-4} for an embryo dose of 5 mSv; the natural risk of such an occurrence is about 1 to 5×10^{-2}. This calculated excess risk is based on the data for external irradiation which may not be strictly applicable to administration of radiopharmaceuticals. However, no appropriate data on the effects of administration of radionuclides are available.

Another problem related to the ten-day principle is the need, or otherwise, to advise a patient of child-bearing age to avoid becoming pregnant for some time after a radiopharmaceutical investigation. No information is available about the effects on pregnancies arising within a very short time after administration of radionuclides but a survey of the published data on females who received therapeutic doses of ^{131}I in childhood indicates that, following gonad doses of 1 to 4.5 mGy, the incidence of severe malformation or of spontaneous abortion was within the natural limits (Taylor, 1981). The spontaneous abortion rate appears to be a sensitive index of damage and a retrospective study of spontaneous abortions and severe abnormalities arising among patients who have undergone investigations with radiopharmaceuticals would be of great interest.

Since at the currently used dosages of most radiopharmaceuticals the dose to the gonads, or an embryo, is unlikely to exceed 3.5 mSv, it would appear that the excess risk of inducing a severe malformation or a cancer is at least one order of magnitude less that the natural risk of such an occurrence. It is suggested therefore that the application of the ten-day principle is not necessary when the expected dose to the gonads or an embryo from the proposed investigation, or series of investigations, will not exceed 5 mSv. Further, on the present evidence there appears to be no clear case for advising a female patient of child-bearing age who receives such a dose to avoid becoming pregnant for any given period after the investigation.

REFERENCES

ELLIS, R. E., NORDIN, B. E. C., TOTHILL, P. and VEALL, N., 1977. The application of the "ten-day rule" in radiopharmaceutical investigations. (Medical Research Council Isotope Advisory Panel: report of a Working Party) *British Journal of Radiology*, *50*, 200–202.

HUSAK, V. and WIEDERMANN, M., 1980. Radiation absorbed dose estimates to the embryo from some nuclear medicine procedures. *European Journal of Nuclear Medicine*, *5*, 205–207.

Nuclear Medicine Communications, 1980. Editorial. *1*, 129–130.

SEAR, R., 1978. Applicability of the "ten-day rule" to radiopharmaceutical investigations. *British Journal of Radiology*, *51*, 59–60.

TAYLOR, D. M., 1979. Radionuclide investigations and pregnancy—protection of the embryo and fetus. *British Journal of Radiology*, *52*, 605–607.

1981. Radiotoxicology of iodine. *Journal of Radioanalytical Chemistry*, (in press).

HOW DANGEROUS IS "DANGEROUS"?

By M. V. Merrick

Western General Hospital, Edinburgh

The maximum acceptable absorbed radiation dose levels recommended in the various codes of practice are intended to give the lowest possible risk to members of the general public, or to radiation workers, neither of whom derive any direct benefit from this radiation. Medical exposure is explicitly excluded. When assessing medical exposure the problem is to balance the risks of acquiring certain information against the risks of proceeding in its absence. For most diagnostic procedures the radiation risks are small compared to all the other factors involved.

The distinction between medical and non-medical exposure is frequently obscured, a particular example of this being the ten-day recommendation. The original wording explicitly states that it should be applied only exceptionally, when the risks of delaying an investigation do not outweigh the risks of delaying treatment. However it has become a general prohibition, reinforced by august bodies who appear to have lost sight of the original objective.

As if this were not bad enough, the evidence that a "ten-day recommendation" is likely to be of net benefit is tenuous, and totally ignores the risks of irradiating ova or semen before fertilization. Indeed one interpretation of the evidence is that, whilst irradiation of the early embryo (before the start of organogenesis) may lead to a raised incidence of spontaneous first trimester abortion, but no detectable increase in abnormalities in the fetuses which survive, irradiation of the unfertilized ovum is associated with an increased incidence of neonatal malignancy. The statistical evidence is weak, but if this proves correct the "ten-day recommendation" is disadvantageous. There is certainly no evidence that its observance is of benefit to the patient.

Proceedings of The British Institute of Radiology

RADIOPHARMACEUTICAL RISKS: A VIEW OF THE PROS AND CONS

By D. H. Keeling

Department of Nuclear Medicine,
Plymouth General Hospital,
Freedom Fields, Plymouth PL4 7JJ

Risks to patients associated with radiopharmaceuticals are not confined to radiation hazards though these inevitably take greatest interest. The radiation risk to populations from medical investigations and therapy becomes a general social problem and the ultimate decisions of acceptability are made by bureaucrats and politicians. As such it will be a political judgment and not a scientific one. Political judgment—as clearly spelled out by Rothschild (1978)—will require and sanction much higher cost per unit of benefit for radiation than it will for road safety, let alone cigarette smoking. Political judgments vary with the times, but at present seem to regard radiation as particularly dangerous and requiring great expenditure. The medical judgment as to whether an individual patient should receive a radiopharmaceutical will be based on totally different criteria though it may be extremely difficult to quantitate accurately.

At present the risks to patients for both morbidity and mortality due to radiopharmaceuticals as ordinarily used are much less from the radiation than from the "pharmaceutical". Adverse reactions to radiopharmaceuticals are almost invariably due to the chemical and physical properties of the material and no (short-term) radiation reactions have been reported for some years: there is little reason to think that the long-term effects will be any different. The present pattern of adverse reactions to radiopharmaceuticals simply shows sporadic cases involving nearly all types of material injected parenterally and are mostly of the idiosyncratic hypersensitive vasomotor and bronchospastic type plus some cutaneous reactions.

There is no doubt that the risk to patients today from radiopharmaceuticals is far greater from the pharmaceutical moiety, including added stabilizers and blocking agents, than from the radionuclidic element.

REFERENCE

ROTHSCHILD, LORD. "Risk". BBC Richard Dimbleby Lecture, 23rd November, 1978 reprinted in *Atom*, No. 268, 1979 (UK Atomic Energy Authority, London), pp. 30–35.

Obituary

Frank Hugo Howarth, M.A., M.B., B.Chir., M.R.C.S., F.R.C.P., D.M.R.D., F.R.C.R.

Dr Frank Hugo Howarth, who was the Senior Consultant Radiologist at the Queen Elizabeth Hospital, Birmingham, died suddenly on New Year's Day, 1981.

Dr. Howarth was born in Pelsall, Staffordshire in July, 1916. Educated at Queen Mary's College, Walsall, he obtained a scholarship to Corpus Christi College, Cambridge in 1935, where in the next three years his academic achievements were quite outstanding. He gained many exhibitions and prizes and was awarded first-class honours in both parts of the Natural Science Tripos. Dr. Howarth was Price Scholar at the London Hospital Medical College from 1938 to 1941 and following house officer appointments at this hospital he joined the R.A.M.C. Between 1942 and 1946, he served with a Field Ambulance in Arakan and Burma and with the 4/9th Gurkha Rifle Special Force, later becoming medical specialist in charge of the medical division of a field hospital, with the rank of Major. Leaving the R.A.M.C. in 1946 he was appointed Registrar to Lord Brain and Dr. R. R. Bomford at the London Hospital.

In 1948 Dr. Howarth entered the specialty of diagnostic radiology to which he later contributed so much. After further apprenticeship at the London Hospital, he was appointed Consultant Radiologist to the Queen Elizabeth Hospital, Edgbaston, Birmingham in 1954. He was later elected F.R.C.P. in 1966 and F.R.C.R. in 1975.

Generations of doctors in Birmingham owe a great debt to Frank Howarth for the wisdom of his teaching, which characteristically was conducted in a quiet and unobtrusive way and often by example as much as the spoken word. His influence on diagnostic radiology was profound and soon after his appointment to Birmingham, Frank became one of the pioneers of the new Seldinger technique in vascular radiology which was to have such wide application in the United Kingdom. Frank combined a formidable intelligence with sound clinical judgement, commonsense and a superb sense of humour. None of us who worked with him or saw him carrying out procedures was ever again content with a mediocre standard of work. As an opinion he was eminently sound; as a colleague he was loyal and considerate; in performing special procedures he was deft and compassionate; as a presenter of cases at medical meetings, he had no equal. It was perhaps in this area that his influence was greatest on a younger generation of radiologists. No-one who has seen clinical data interpreted and handled so skilfully could fail to be impressed, enlightened and given a new outlook on the scope of diagnostic imaging. Frank remained so well informed about developments in medicine that in the last year of his life he became competent in CT scanning and ultrasonography.

Although Frank's professional contribution to diagnostic radiology can hardly be overestimated, he will above all be remembered with affection as a colleague and friend. It is difficult to imagine a man who had so many friends and the number of people who attended his funeral bore testimony to this.

Those of us who work in the Queen Elizabeth Hospital find it hard to believe that he has been taken from us. We shall miss the quick footstep in the Department, the ready smile, the cheerful word for all, the sound clinical opinion and above all, the calm appraisal of a situation in which a younger colleague so often needs the advice of an older and wiser man. To his charming wife, Lucy, and to his sons, Peter and David, we extend our greatest sympathy.

Frank's influence will last, and surely it can be said of him, as was said of Heraclitus so long ago:

> "Still are thy pleasant voices, thy nightingales, awake;
> For Death, he taketh all away, but them he cannot take."

F. G. O. BURROWS.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

1982 George Simon Memorial Fellowship Award

Entries are invited for the 1982 George Simon Memorial Award which will be given for the best original work relating to radiologic or other imaging of the respiratory system. The award consists of a trip to the Fleischner Society Meeting and Course, with all expenses paid, plus a cash prize. In 1982, the meeting and course will be held in Austria, in May. The Fellowship Award recipient will present the submitted work at the Society meeting. Although the Fellowship Award paper can be the result of work done by several investigators, the senior author should be the applicant and responsible for the majority of the work. Papers published or already submitted for publication will not be eligible for this award. Applicants should not be older than 40 years of age.

Submissions for the 1982 award must be in the form of a complete scientific paper, not longer than twenty-five (25) pages (typed double-spaced), and should be sent in triplicate to Richard H. Greenspan, M.D., Department of Diagnostic Radiology, Yale University School of Medicine, 333 Cedar Street, New Haven, Connecticut, 06510, on or before December 1, 1981. Further information is available upon request.

BIR Meetings, May 1981

Thursday, May 14: State of the Art Seminar on Preparation of the Bowel Prior to Radiology (Chairman, Dr. G. J. de Lacey) at 17.45; and Radiology of the Colon (speakers: C. Bartram, C. Wastell, C. Williams) at 19.40. Friday, May 22: Radiobiology work-in-progress meeting on Hyperthermia, at 11.00.

Annual General Meeting

The Annual General Meeting of the Institute will be held on Thursday, May 14, 1981. All members will receive notification.

Fourth European Congress on Ultrasonics in Medicine

This will be held in Dubrovnik, May 17–24, 1981, sponsored by EFSUMB and organized by the Yugoslav Association of Societies for Ultrasound in Medicine and Biology. Information from Dr. Višnja Latin, M.D., D.Sc., President of the Organizing Committee, Jagode Truhelke, 26, 41090 Zagreb, Yugoslavia.

The Marie Curie Memorial Foundation, London
Thirteenth Annual Symposium
Cancer—A Panoramic View

Thursday, May 28, in the Edward Lumley Hall, the Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2A 3PN. Chairmen: Mr. R. W. Raven and Dr. F. J. C. Roe. Other speakers: Prof. D. V. Parke, Prof. R. W. Baldwin, Mr. R. Tiffany, Prof. A. Lant, Dr. N. Finter, Prof. K. Hellmann, Dr. I. W. F. Hanham and Mr. I. Burn. Fee £10·50. Applications and information: Mr. G. D. Steward, Assistant Secretary, The Marie Curie Memorial Foundation, 124 Sloane Street, London SW1X 9BP (phone 01-730 9157).

Fourth Symposium on Neutron Dosimetry

Organized jointly by the Commission of the European Communities and the Society for Radiation and Environmental Research GSF in Munich-Neuherberg on June 1–5, 1981.

Topics are: neutron sources, radiation transport calculations, dosimetry and spectrometry, neutron risk assessment, radiation protection concepts.

Corresponding secretary: G. Burger, Gesellschaft für Strahlen- und Umweltforschung mbH München, Ingolstädter Landstraße 1, D-8042 Neuherberg, telephone: 089-38 741.

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Programme from: ICR81, c/o Brussels International Trade Fair, Parc des Expositions B-1020, Brussels, Belgium.

First International Symposium on Minimal Invasive Cancer

Organized by the University Clinic of Obstetrics and Gynaecology, Graz, Austria, to be held at the Kongresshaus, Graz, July 1–4, 1981. Language: English. Main topics: cervix, vulva, endometrium, breast, oesophagus, stomach, large intestine, lung, thyroid, urinary bladder, prostate, larynx, oral cavity, skin, other organs. Enquiries: Interconvention, PO Box 105, A-1014, Vienna, Austria (phone (0222) 57 62 88). President: Prof. E. Burghardt; Secretary General, Dr. E. Holzer.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

International Symposium and Course on Abdominal Ultrasound

Turku, Finland, August 10–12, 1981, organized by the Radiological Society of Finland and the European Association of Radiology. Language: English. Guest speakers: C. R. Hill, H. H. Holm, M. Johnson, A. Kratochwil, C. Metreweli, E. H. Smith and F. Weill. Two "free communications" sessions, for which 10 minute papers are invited: abstracts to be submitted with registration. Technical exhibition and social programme. Information and registration: Oy Konfer Ab, Yliopistonkatu 29 c B, SF-20100 Turku 10, Finland.

Contrast Media. Fundamentals and Clinical Application

The Department of Diagnostic Radiology of the University of Rochester will offer a two-and-a-half day course on Contrast media: fundamentals and clinical application, September 21–23, 1981. The philosophy of this course is to review the fundamental chemical, physical, physiological, and toxicological properties of radiopaque media and to describe the relationship and importance of these properties to radiological application and diagnoses. The curriculum will provide a thorough introduction to contrast media for residents, Fellows, and junior faculty as well as a refresher course for the more experienced radiologist. The knowledge conveyed should be useful in the clinical setting and in the laboratory. For further information, contact Harry W. Fischer, M.D., Chairman, or Michael R. Violante, Ph.D., Course Director, Department of Radiology, PO Box 648, University of Rochester Medical Center, Rochester, New York 14642; phone (716) 275–2617.

Skeletal Radiology

The Eighth Refresher Course of the International Skeletal Society will be given in Madrid, Spain, September 25–27, 1981.

For further information, please write to: A. Bonakdarpour, M.D., Department of Diagnostic Radiology, Temple University Hospital, 3401 North Broad Street, Philadelphia, PA 19140, USA; or Prof. Dr. Friedrich W. Heuck, Zentrales Röntgeninstitut, Katharinen Hospital der Stadt Stuttgart, Kriegsbergstrasse 60, Stuttgart 1, Germany.

European Association of Radiology
II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

The Faculty of Radiologists of The Royal College of Surgeons in Ireland

21st Anniversary Meeting, Dublin, October 2–3, 1981: jointly with The British Institute of Radiologists, The Royal College of Radiologists, and The Royal Society of Medicine. Diagnostic and therapy sessions; topics to include radiology in renal failure and radiology of trauma. The BIR Presidential Address for 1981, "Chest radiology—guesswork or science?" will be given by Dr. D. H. Trapnell. Technical exhibition. Details: Miss A. Daly, Faculty of Radiologists, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2.

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

The Short and Long Term Biological Consequences of Exposure to Radiation

Middlesex Hospital, London. Tuesday, October 13, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

Symposium on Education and Training in Radiobiology

Dresden, May 12–15, 1982. Organized by the Gesellschaft für medizinische Radiologie der DDR, under the auspices of the European Society of Radiology. Languages: English, French and German. Registration by December 1, 1981; papers by August 15, 1981. Information: Professor R. Barke, Radiologische Klinik, DDR – 8019, Dresden, Fetscherstrasse 74.

Society for Radiological Protection
Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ. Abstracts to be received by July 15, 1981.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01–486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

Erratum

The use of diagnostic ultrasound to measure the lumbar spinal canal

In the caption to Fig. 1A of the letter from J. A. Veiga-Pires *et al.* (The British Journal of Radiology, March 1981, *54*, 269), the AP diameter should have read 12.4 mm (16.0 mm normal), not 12.4 cm (16.0 cm normal).

Book reviews

Physics in Nuclear Medicine. By J. A. Sorenson and M. E. Phelps, pp. vi+404, 1980 (Grune and Stratton, New York), $39.50.
ISBN 0-8089-1238-0

This is a most comprehensive volume, designed for use as a course book by students of nuclear medicine. In the Preface the authors state: "We have attempted to be thorough and accurate in our discussions of important basic principles, believing this approach to be of more permanent value than a superficial or over-simplified one designed to make these complex topics 'palatable' to the student or trainee". Reading the book one gets a feeling of not being rushed. Fourteen chapters of material precede the first of two chapters on the gamma camera. They include a chapter on problems in radiation detection and measurement, as well as one on pulse height spectrometry. These are in addition to those on radiation detectors, on electronic instrumentation for radiation detection systems, and two chapters on counting systems. The gamma-camera chapters are followed by one on other imaging techniques and instruments, including section scanning, and a general chapter on image quality. The material is thus delivered in reasonably small amounts and the aim of thorough and careful treatment is attained. Familiarity with basic mathematics is assumed, and some students will need a helping hand.

The early parts of the book may be criticized on the grounds that some definitions are given in a rather loose fashion, *e.g.* "The half life of a radionuclide is the time required for it to decay to 50% of its initial activity level". It also includes the traditional, but to me unhelpful, graph showing the variation of output pulse height with applied voltage for gas filled detectors. This is labelled as usual with recombination, ionization, proportional and Geiger regions. This seems to imply that one can obtain all these different modes of operation from the same device and that an ionization chamber delivers pulses. The section on the mode of operation of the analogue rate meter is also misleading. Apart from these few blemishes, however, the book succeeds very well. The material is most expertly put over and much time must have been expended in making the descriptions clear. Worked examples are included in the text where appropriate, and where a topic becomes too complex useful references are given. Some users will be sad that SI units are defined but not used in the text. However, the book is more about technical matters than quantities of radioactive material, and I do not feel this to be a serious problem. This up-to-date book will be welcomed by physics teachers of nuclear medicine courses for radiographers, clinicians and physicists.

N. J. G. BROWN.

Introduction to Cerebral Angiography. By Anne G. Osborn, pp.xi+436, 1980 (Harper & Row, London), £28·00.
ISBN 06-141829-?

This monograph by a single author provides a fundamental, relatively comprehensive text and atlas of cerebral angiography. It is well written in a pleasing style, providing a wealth of factual information supported by a good selection of references and a detailed index. The illustrations are superb; the angiograms are presented as subtraction prints and they are labelled and supplemented with line drawings. Though used lavishly they have been carefully selected and none are redundant.

The book goes well beyond the requirements for the F.R.C.R. and it is strongly recommended to trainees in neuroradiology and the other neuro-sciences.

B. E. KENDALL.

Radiology of the Urinary System. By Milton Elkin. Vol. I pp. xix+688, Vol. II pp. xi+678, 1980 (Little, Brown, Boston). $55.00 each.
ISBN 0-316-23275-0
0-316-23276-9

This textbook is based on uroradiological experience accumulated at the Albert Einstein College of Medicine during some 25 years. Professor Elkin has been joined by six contributing authors from his own staff and by Professor Joshua Becker from New York State University. The resultant authoritative account of the whole of the subject is full of facts presented with sound common sense and supported by an excellent review of the world literature.

The seventeen chapters are divided on largely conventional lines but include one on positional abnormalities of the urinary tract and another on kidney size. Preparation of the book was apparently well advanced when computed tomography, nuclear medicine and ultrasound burst on the scene, and these topics are presented in separate chapters and not incorporated adequately in the remainder of the book. There is a wealth of information regarding the definition of diseases in the urinary tract, their aetiology and pathology; by comparison, the radiological signs are less fully evaluated. The script is written in a conversational style and tends to be repetitive, most aptly perhaps in the account of duplication and triplication of the urinary tract. Not all the references are cited in the text and those that are tend too often to be reviewed in an uncritical way without the author giving the reader the benefit of his personal view. The illustrations are of only moderate quality, but do include numerous examples of rarer conditions which have been donated by colleagues. Inevitably there are occasional comments which are open to challenge, *e.g.* it is held that carcinoma in a bladder diverticulum is a coincidental event and the effects of stasis with persistance of intermittently excreted carcinogens are ignored. There is also an implication that American bladders are of small volume, because in the account of the infrequent voider syndrome it is stated that "Large amounts of fluid—400 mls in an adult—can be instilled into the bladder without discomfort"!

Overall this is a valuable contribution to the urological literature. It illustrates very clearly the tendency for authors of textbooks of radiodiagnosis to concern themselves primarily with radiological pathology. Undoubtedly such pathology must form the basis of all diagnosis and for this reason the book can be warmly commended to radiologists of all levels of experience.

J. ROYLANCE.

Therapeutic Progress in Ovarian Cancer, Testicular Cancer and the Sarcomas Ed. A. T. van Oosterom, F. M. Muggia and F. J. Cleton, pp. xv+506, 1980 (Martinus Nijhoff, The Hague; Leiden University Press), Guilders 125.
ISBN 90-6021-452-8

This volume contains the proceedings of a meeting held in December 1979 organized by the Boerhaave Committee for postgraduate medical education through the Faculty of Medicine, University of Leiden and the Mount Sinai School of Medicine, New York. The four types of solid tumour covered at this meeting, ovarian carcinoma, testicular tumours, osteosarcoma and soft-tissue sarcomas, have each been the subject of recent claims for improvements in treatment. The editors and most of the contributors clearly have a particular interest in cytotoxic chemotherapy but other aspects, such as tumour biology, diagnostic techniques, surgery and radiotherapy, are adequately represented.

The first section, on ovarian carcinoma, emphasizes the importance of an adequate staging laparotomy and makes the case for cytoreductive surgery in advanced tumours and second-look laparotomy. In patients with no residual macroscopic disease, radiotherapy to the whole abdomen appears to give better results than chemotherapy. The results of treatment of patients with advanced tumours by a number of chemotherapy combinations appear attractive but there is little quantitative information on drug toxicity. It is perhaps still too early to conclude whether the improvement in response rate with combination chemotherapy is justified in view of the added toxicity encountered.

The treatment of testicular teratomas is well presented in the next section. The excellent results with early staged disease, and recently improved results in more advanced disease, with chemotherapy are well documented. Recent changes in treatment have made this a highly specialized field; the panel discussion in particular gives a useful account of the background of these developments.

The section on osteosarcoma gives a full account of the pathology and treatment but unfortunately no radiographs are included. The trials of adjuvant chemotherapy and immunotherapy use historical controls and it is possible that recent improvements in treatment, such as surgical resection of pulmonary metastases, may also be contributing to increased survival. However, clinical trials are obviously still preferable to "*ad hoc* treatment".

The major part of the final section on soft-tissue sarcoma is devoted to combination chemotherapy, and inevitably the numbers involved are small and follow-up periods are short. There is scant reference to the use of radiation to reduce local recurrence, and statistical confirmation of the efficacy of adjuvant chemotherapy or radiotherapy is still lacking.

All four sections of the proceedings have a tendency to emphasize the role of chemotherapy but the discussion and conclusions present a balanced view of current management. Since these proceedings demonstrate the need for collaboration in studying the treatment of malignant tumours, perhaps specialists in different fields of oncology will be encouraged by this book to continue participating in such clinical trials.

V. Barley.

Thermal Characteristics of Tumors: Applications in Detection and Treatment. Ed. R. K. Jain and P. M. Gullino. 1980. pp. 542 (New York, Academy of Sciences), $95.00.
ISBN 0-89766-046-3

There are two kinds of books of proceedings: this is one of the sort that results from intelligently planning a meeting and the corresponding book around a timely and stimulating topic. Over the past decade there has been a great acceleration of systematic interest in the thermal behaviour of tumours, partly in relation to aspects of tumour biology and partly from applied interests in both diagnosis and therapy. This book brings the whole subject together with a series of about forty generally well-written and authoritative papers. The topics covered include tumour physiology, particularly in relation to blood supply, mathematical and physical studies of bio-heat transfer, physical techniques for induction of hyperthermia by whole body and regional perfusion and radiation methods, methods of measurement of tumour and skin temperature, cell and mammalian thermobiology, and trials of clinical hyperthermia in both stand-alone and adjuvant applications. A common thread that runs through much of all this is blood supply, with the very exciting possibility that, by possessing characteristic abnormalities in their vasculature, tumours may both offer clues for their detection and also present what Dickson, in his summary paper, suggests might be "a genuinely exploitable Achilles heel for cancer therapy".

This is not an easily digestible book, nor one that should be read uncritically, but it can be recommended for anyone—therapist, physicist or biologist—with an enquiring interest in the subject, and will be for some time to come a necessary reference source for serious researchers.

C. R. Hill.

Renal Adenocarcinoma. Ed. G. Sufrui and S. A. Berkley. A series of workshops on the biology of human cancer. Report No. 10—UICC Technical Report Series, Vol. 49 pp. 215. 1980. (UICC, Geneva), Sw.F. 17.00.
ISBN 92-9018-049-8

This softback publication is based on the proceedings of a recent UICC sponsored workshop, the purpose of which was to review and identify promising areas for future research which might help us cope with this serious tumour.

The publication is a concise and useful summary of present thought from a wide range of research fields and ends with a chapter on conclusions and recommendations for future study. Throughout, the direct relevance of all the research to the clinical scene is very apparent so that the book is easy to read and understand. It should therefore appeal to all who have connections in their work with this particular tumour.

B. T. Hale.

Radiographic Photography and Imaging Processes. By D. Jenkins. pp. vii+302, illus. 1980. (MTP Press Ltd, Lancaster), £11·95.
ISBN 0-85200-208-4

Although photography has long featured as a separate entity in the syllabuses for training radiographers and radiologists, this is the first satisfactory monograph dedicated to the subject. The title includes the words "Imaging Processes," but nuclear medicine, ultrasound and CT have been excluded as the author feels these are too specialized and each deserves a separate book. There are 16 chapters which cover all aspects of film, exposure and processing. The practice and underlying theory of image production, tests for quality control and the management of film stocks are all discussed in depth.

The text well reflects the ability of the author, founded as it is on a long experience in both practical radiography and in teaching. An interesting subject has been made even more interesting and, despite the author holding a degree in mathematics, or perhaps because of this, the mathematical content of the book has been kept to a minimum and has been made very clear. The diagrams and illustrations have been well selected and are beautifully reproduced. There is an adequate index but no formal bibliography.

The author is to be congratulated on the quality of this first edition which will surely become obligatory reading for all students of radiology and radiography. Not only should libraries of teaching units acquire this book, but all students and teachers must be urged to purchase their own copies.

J. Roylance.

Radiologic Science for Technologists. Physics, Biology and Protection. By Stewart C. Bushong. 2nd ed., pp. xi+503, 1980 (YB Medical Publishers, Chicago/London), £15·50.
ISBN 0-8016-0928-3

This is a very comprehensive book, in which the author has brought physics, equipment and photography together in one volume. It consists of nearly 500 pages and contains many photographs and illustrations, and is well presented and comes with a hard-back cover. Professor Bushong, who has been teaching students for a number of years, describes his book very aptly as a text in radiologic science. This is in fact the second edition, the first having been published in 1975, and it is based on the curriculum guide of the American Society of Radiologic Technologists.

The author believes that "physics is fun" and goes to a lot of trouble to make the text understandable, and this care is evident throughout the book. At the end of each chapter there is a series of review questions. The book is designed for use with worksheets for the student, and, for the teacher, an instructor's manual giving details of laboratory experiments.

In a book which covers such a wide field I would have liked to see more information provided on automatic processing, but there are detailed chapters on computed tomography, xeromammography and ultrasound, while much emphasis is placed on radiobiology and radiation protection.

My overall impression is that here is a well-written textbook, which, with the author's very extensive survey of all aspects of imaging in an X-ray department, must surely be of assistance to the student.

R. H. Bryan.

1001 Questions About Radiologic Technology. Vol. 1. By R. Bell, pp. 173, 1980 (University Park Press, Baltimore), £4·25.
ISBN 0-8391-1607-1

According to its stated purpose, *1001 Questions About Radiologic Technology* "is useful in helping the student discover weaknesses in specific study areas." The book succeeds in fulfilling this purpose. The author has divided the questions into two main sections covering all aspects of radiography. The answers are clearly listed at the back of the book together with a list of textbook references. The questions are also cross-referenced to these textbooks for easy study.

This book would be a useful addition to a radiography school library and for the students to use as part of an interaction revision programme. But The College of Radiographers' proposed multiple-choice examinations are scheduled to use two types of questions: the single answer only, the AK5 type questions, and the combination answer, the AK3 type question. This book only includes the former and therefore has limited use in the British system.

Mary J. Lovegrove

Repères et Mesures en Radiodiagnostic. By A. Coussement, C. Fauré and N. Coussement-Beylard. 3rd ed., pp. 316, 1980 (Expansion Scientifique Francaise, Paris), 192 Fr.
ISBN 2-7046-1048-7

This French book of radiographic measurements is well presented, filled with line drawings—but no radiographs—and packed with hard information obtained from the English speaking and European literature.

It is not likely, however, to be of any use to British radiologists or radiographers as it is very similar to the already well known *Atlas of Roentgenographic Measurement* by L. B. Lusted and T. E. Keats. The only significant difference between these books is the longer section on CNS measurements in the French book. A very large number of drawings are exactly the same, many sections are set out in such a similar fashion that they appear as duplicates, the source material for these sections being identical.

I do not see a place for this bench book in our market.

J. C. Parker

Effects of Irradiation on the Small Intestine of the Rat. A SEM Study. By Lars-Gösta Friberg, pp. 235, 1980 (Lund University Press, Sweden), $15.00.
ISBN 91-7222-298-0

This is another good example of the continental custom of publishing a doctoral thesis in a professionally printed form suitable for much wider circulation than is the case with British university theses, which rarely see the light of day after the candidate has been examined. In this particular case the book is especially useful because of the large number of illustrations it contains, including over 300 scanning electron micrographs (SEM). Most doctors seek to publish the highlights of their thesis in the open literature, but journal editors place a severe restraint upon the number of illustrations in such papers, and most of the material remains hidden in the university library.

The photographs are very well reproduced and show the mucosal surface of the small intestine of the rat at various times after various single and fractionated doses of ^{137}Cs γ rays delivered to the abdomen. Friberg then attempts to quantify the radiation damage to the villi, the epithelial cells and the microvilli on the cell surface using the sort of 0–4 scale that reminds one of Fowler's scale for skin damage. Such arbitrary scales have been criticized because they are "non-parametric" but I have some sympathy with the method, since my former Glasgow colleagues and I have used an analogous scoring system in our own SEM studies of mouse small intestine.

How else can one quantify radiation damage to a complex tissue which performs the contrary functions of absorbing the digested elements of the diet and preventing the passage of lethal bacteria? A number of the photographs show such bacteria "attacking" swollen villi 48 hours after irradiation. Such pictures provide an education in themselves and indeed the whole book justifies a place in every medical library regardless of the radiation topic.

My one disappointment was the author's conclusion that iso-effect curves could not be plotted from all his fractionation data. If his scoring system is valid then it ought to be possible to make more use of it than his single diagram of Strandqvist type curves, each based upon only two points. These studies of the surface of the small intestine are important to radiotherapists and their radiobiology colleagues who must realize that the counting of regenerating crypts can only provide part of the explanation why the gut is such an important dose-limiting normal tissue.

A. H. W. Nias.

Books received

Receipt of the following is acknowledged as a courtesy to the senders. They have been lodged in the library of The British Institute of Radiology for the use of members.

TNM Classification of Malignant Tumours. A Brochure of Checklists. 1st ed. UICC Technical Report Series 51. Looseleaf folder 50 pp. (International Union Against Cancer, Geneva), Sw.fr.20.
ISBN 92-9018-051-X

Management of Thoracic Trauma Victims. Ed. J. K. Trinkle and F. L. Grover, pp. 109. 1980 (Lippincott, Philadelphia), £7·75.
ISBN 0-397-50415-2

High dose-rate after-loading in the treatment of cancer of the uterus

Edited by Thelma D. Bates and Roger J. Berry

British Journal of Radiology Special Report 17

For more than fifty years intracavitary irradiation has formed a major part of the treatment of cancer of the cervix and corpus uteri. In recent years high dose-rate remote after-loading devices have been developed which have removed all radiation hazards to medical and ancillary staff and other patients, but until now the question "Are the clinical results achieved by high dose-rate after-loading intracavitary treatment of carcinoma of the cervix and corpus uteri at least as good as those achievable by conventional low dose-rate intracavitary techniques?" had not been answered by adequate clinical experience. At a meeting held at The Middlesex Hospital Medical School, London from 10–12 April 1978, 86 participants and observers from 36 Hospital Centres in 15 countries gathered to discuss relevant physics and radiobiology studies and to pool their clinical experience in the use of high dose-rate after-loading devices. This volume presents brief versions of their 33 contributed papers and a distillation of the lively discussion which took place. Although the conclusions reached were necessarily cautious, lest future results not reflect those already achieved, those so far with remote high dose-rate after-loading appear to be in no way inferior to the results of traditional methods. In fact there are indications that high-dose fractionated intracavitary therapy may be associated with a lower incidence of normal tissue complications for a comparable level of achievement of tumour local control in cancer of the cervix and corpus uteri.

High dose-rate remote after-loading devices have the ability to treat very large numbers of patients, and have a particularly valuable contribution to make in the treatment of these distressingly common cancers in developing countries. This volume provides comprehensive views of clinical and radiobiological experience for those centres acquiring or considering high dose-rate after-loading equipment.

ISSN : 0306–2120
ISBN : 0–905749–07–3 Price **£15**

Orders to :
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
(01–935 6237) or through your bookseller.

Clinical and Experimental Applications of Krypton 81m

Edited by J. P. Lavender

British Journal of Radiology, Special Report 15.

This work is composed of papers presented at an International Meeting held in June 1977 concerned with a new physiological tool; the use of a very short-lived radioactive gas krypton 81m.

Krypton 81m is a noble gas with a 13 second half life available from a portable generator with a half life of 4½ hours. Although known for a number of years it has only been used with any frequency by physiologists and clinicians since 1975.

The first section of the book deals with the production of the parent isotope rubidium 81 and the design of generators. The second section comprises a series of papers concerned with the use of the equilibrium image as both a picture and a measure of regional lung ventilation and perfusion. It also outlines problems of deriving absolute values of lung function. In the third section, papers illustrate the use of krypton 81m as a clinical tool in the diagnosis of pulmonary embolic disease and other pulmonary diseases and compare such information with that obtained from the more familiar xenon 133. In the last section the use of intra-arterial krypton as a marker of regional myocardial and cerebral blood flow is discussed. This technique, which has been most highly developed in the case of the myocardium, allows detailed images of the myocardial perfusion to be recorded. Perhaps its clearest application is in following rapid changes of regional myocardial perfusion in response to transient ischaemia, stress and drugs.

The discussion following each paper allows an assessment of the value and place of this new technique.

ISBN 0 905749 01 4
ISSN 0306–2120 Price **£12**
Orders to :
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
(01–935 6237) or through your bookseller.

Carcinogenesis and Radiation Risks: a Biomathematical Reconnaissance

by W. V. Mayneord, C.B.E., D.Sc., F.R.S. and R. H. Clarke, Ph.D.

with foreword by Sir Eric Pochin, M.D.

British Journal of Radiology Supplement No. 12, 1975; reprinted 1979.

The first printing of this refreshingly original monograph by Professor Mayneord and Dr. Clarke was sold out. In view of the increasing interest in the topics dealt with by the authors, the work was reprinted. It explores some of the fundamental problems that arise when one attempts to predict the biological effects of a given dose of radiation. The authors point out that, in attempting an estimate of biological effect, for example carcinogenesis, it is frequently assumed that the risk is simply proportional to the dose received, although biological experiment often reveals a much more complex relation between effect and dose. They examine some of the consequences of taking such complex relationships into account in assessing "risk" on the basis of "dose" and propose a formula relating the risk to a whole population of cells from a rare event, such as the "transformation" of a single cell or group of cells. The parameters of the basic formula can be varied to meet particular assumptions regarding the distribution of dose in tissue and of response to dose. Using this formula, analyses are made of many different types of problem, including those presented by "point sources". It is emphasized throughout that the derivation of probabilities is not merely an exercise in mathematical physics but also involves cytology, genetics, immunology and hormone physiology, as well as studies of viral and chemical carcinogenesis. However, the method of analysis used leads to a clearer definition of the problems that have to be studied in attempting to produce more logical estimates of the risks from radiation, and the quantities of significance in designing experimental investigations.

The monograph represents a detailed development of ideas presented by Professor Mayneord in his Mackenzie Davidson Memorial Lecture of 1968 on "Radiation Carcinogenesis" and workers in the fields of radiobiology, experimental carcinogenesis and health physics will gain valuable insights from this study.

Orders to: Price **£6·50**

Publications Department, The British Institute of Radiology,
32 Welbeck Street, London, W1M 7PG (01–935 6237) or your bookseller.

Book reviews

Radiation quantities and units 380

Alimentary tract radiology 397

Atlas of the human brain for computerized tomography 402

Correlative neuroradiology 402

Quality assurance of radiopharmaceuticals 427

Physics in nuclear medicine 438

Introduction to cerebral angiography 438

Radiology of the urinary system 438

Therapeutic progress in ovarian and testicular cancer and sarcomas 438

Thermal characteristics of tumours 439

Renal adenocarcinoma 439

Radiographic photography and imaging processes 439

Radiologic science for technologists 439

1001 questions about radiologic technology 440

Repères et mesures en radiodiagnostic 440

Effects of irradiation on the small intestine of the rat 440

Books received 440

St. James's University Hospital, Leeds

2nd Annual Course on

Diagnostic Imaging

2–6 November 1981

A one week Course in Diagnostic Imaging will be held at St. James's University Hospital, Leeds. The Course will emphasise the competitive and complementary aspects of radionuclide imaging, computed tomography and ultrasound in clinical usage, and will be aimed at senior registrars in imaging specialities and consultants with interests in non-invasive imaging techniques.

The fee for the Course is £80.00 which includes lunches and morning and afternoon refreshments.

Residential accommodation can be arranged if required at a central hotel.

Early application is advised.

Full details together with programme and application form can be obtained from Mr. Frank Moran, Senior Administrative Assistant, Postgraduate Dean's Office, Littlewood Hall, Leeds General Infirmary, Leeds LS1 3EX.

Guidelines for the Preparation of Radiopharmaceuticals in Hospitals

Revised 1979 edition

BIR Special Report No. 11.

First produced 1975, this was amended to comply with revised UK safety legislation.

Publications Department,
British Institute of Radiology,
32 Welbeck Street,
London W1M 7PG

SPECIAL PRICE: 50p (postage and packing extra)

VOL 54 NO 641 MAY 1981

The British Journal of Radiology

Contents

Page

Conversion to SI units in radiology. 377
BIR Working Party on SI Units

How much do you know about quantities and units? 381
W. A. Jennings

Age-related brain atrophy and mental deterioration—a study with computed tomography. 384
M. Ito, J. Hatazawa, H. Yamaura and T. Matsuzawa

Resolution of multiple hepatic abscesses following percutaneous transhepatic biliary drainage. 391
R. R. Mason and J. D. Irving

Ultrasound guided percutaneous abdominal abscess drainage. 394
D. P. MacErlean, A. P. Owens and J. B. Hourihane

Modification of gallium-67 citrate distribution in man following the administration of iron. 398
F. W. Smith and P. P. Dendy

Synthetic porphyrins as tumour-localizing agents. 403
G. D. Zanelli and A. C. Kaelin

Technical notes. 408
  Myelographic study of the obstructed spinal theca with water-soluble contrast medium.
    B. E. Kendall and A. R. Valentine
  Improved radiotherapeutic technique for prophylaxis of the central nervous system in patients with acute lymphoblastic leukaemia.
    M. Pla, E. B. Podgorsak, T. H. Kim and C. R. Freeman

Case reports. 416
  An unusual case of neurofibromatosis: cystic bone lesions and coarctation of the aortic arch.
    I. Beggs, D. G. Shaw, D. P. Brenton and C. Fisher
  A large bowel lymphoma complicating renal transplantation.
    D. N. M. Coggon, D. H. Rose and I. D. Ansell
  Therapeutic embolization of phaeochromocytoma.
    J. B. Timmis, M. J. Brown and D. J. Allison
  Arteriography of Castleman tumour of the mesentery.
    T. E. Gudmundsen and A. Kolbenstvedt
  The anomalous inferior vena cava—another structure between the aorta and the superior mesenteric artery.
    A. Kolbenstvedt, F. Kolmannskog and H. H. Lien
  Post-biopsy haematuria successfully treated by selective transcatheter epinephrine injection.
    N. Vaeusorn, J. Viranuvatti and L. Singchoovong
  Osteopathia striata with sclerosis and thickening of the skull (*Addendum*).
    M. R. Paling, I. Hyde and N. R. Dennis

Correspondence. 428
  Occult pneumothorax.
    A. Cohen
  A cautionary note on the use of thiol compounds to protect normal tissues in radiotherapy.
    J. Lunec, Beulah Cullen, Hilary Walker and Shirley Hornsey
  A comparison between two hysterosalpingographic contrast media—Urografin 370 and Isteropac.
    G. H. Whitehouse and C. Sausman
  The use of diagnostic ultrasound to measure the lumbar spinal canal.
    D. Ottewells and P. Howells
  Erratum: The use of diagnostic ultrasound to measure the lumbar spinal canal. 437
    J. A. Veiga-Pires, R. v. d. Beek and M. C. Kaiser

Proceedings of The British Institute of Radiology. 431
  Dosimetry and risks to patients in radiopharmaceutical investigations.

Obituary: Dr. F. H. Howarth. 435

Forthcoming events and notices. 436

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
32 Welbeck Street, London W1M 7PG

ISSN 0007-1285
16482

14.9.82

Volume 54 umber 642
June 1981

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis

[illegible]

and related specialities

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01-836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01-935 6237 and 01-935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

Which company offers superior multi-axis vascular imaging equipment today ...and tomorrow?

General Electric Company of U.S.A:*
Making new technology accessible.

The unique isocentric design of today's L/U-Angio multi-axis vascular system keeps anatomy centered as the equipment is moved from projection to projection...without repositioning the patient. And, this advanced positioning system's Fluoricon L300 image intensifier is fully compatible with digital fluoroscopy technology, to permit optimum clinical performance far into the future.

Such upgrade capability is also designed into other General Electric of U.S.A. imaging systems: In computed tomography, the Continuum concept means that new capabilities can easily be added to every existing CT/T system. And in nuclear diagnostics, by adding a data acquisition and analysis system to an existing MaxiCamera 400T system, complete Emission Computed Tomography can be performed.

Upgrade capability. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

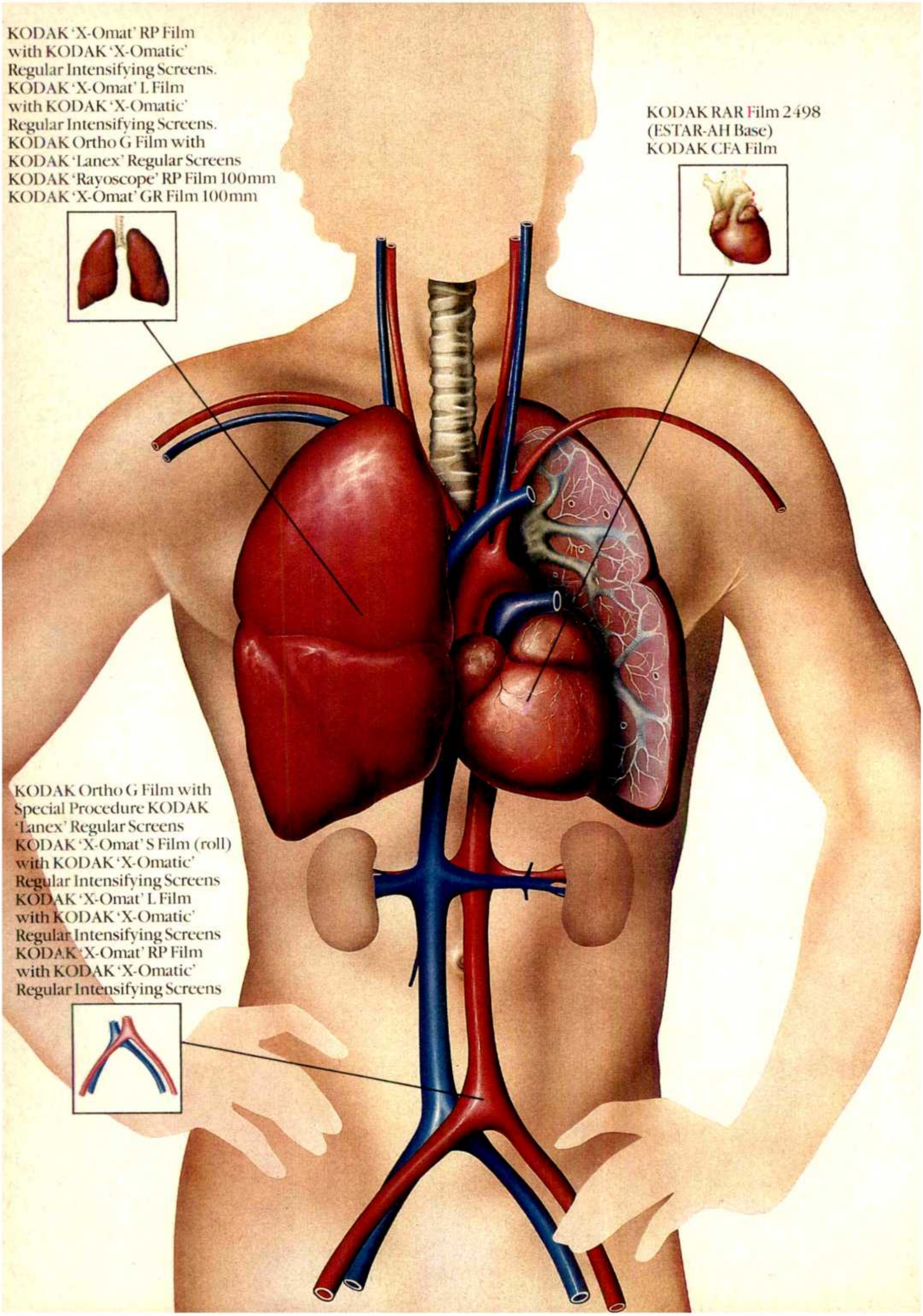
At the leading edge of imaging technology.

For more facts about diagnostic imaging equipment, visit the General Electric U.S.A., exhibit at the International Congress of Radiology in Brussels, June 24 - July 1, or telephone:

International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.



KODAK 'X-Omat' RP Film
with KODAK 'X-Omatic'
Regular Intensifying Screens.
KODAK 'X-Omat' L Film
with KODAK 'X-Omatic'
Regular Intensifying Screens.
KODAK Ortho G Film with
KODAK 'Lanex' Regular Screens
KODAK 'Rayoscope' RP Film 100mm
KODAK 'X-Omat' GR Film 100mm

KODAK RAR Film 2498
(ESTAR-AH Base)
KODAK CFA Film

KODAK Ortho G Film with
Special Procedure KODAK
'Lanex' Regular Screens
KODAK 'X-Omat' S Film (roll)
with KODAK 'X-Omatic'
Regular Intensifying Screens
KODAK 'X-Omat' L Film
with KODAK 'X-Omatic'
Regular Intensifying Screens
KODAK 'X-Omat' RP Film
with KODAK 'X-Omatic'
Regular Intensifying Screens

An outline of Kodak products for cardio-vascular examination.

Kodak has the most comprehensive service network in the country.

We back that service with a range of products that includes over thirty diagnostic imaging films; and covers processors, cassettes, intensifying screens, chemicals and daylight handling equipment.

Kodak Service is there to help you maintain consistent image quality.

In the working environment, this means we can aid with planning an efficient process area.

In human terms, we can help with the training of radiologists, radiographers and technicians: on your premises or at our own Marketing Education Centre.

Equipment maintenance is also an important quality control factor, and Kodak provides a highly competitive service from strategically located Sales Centres.

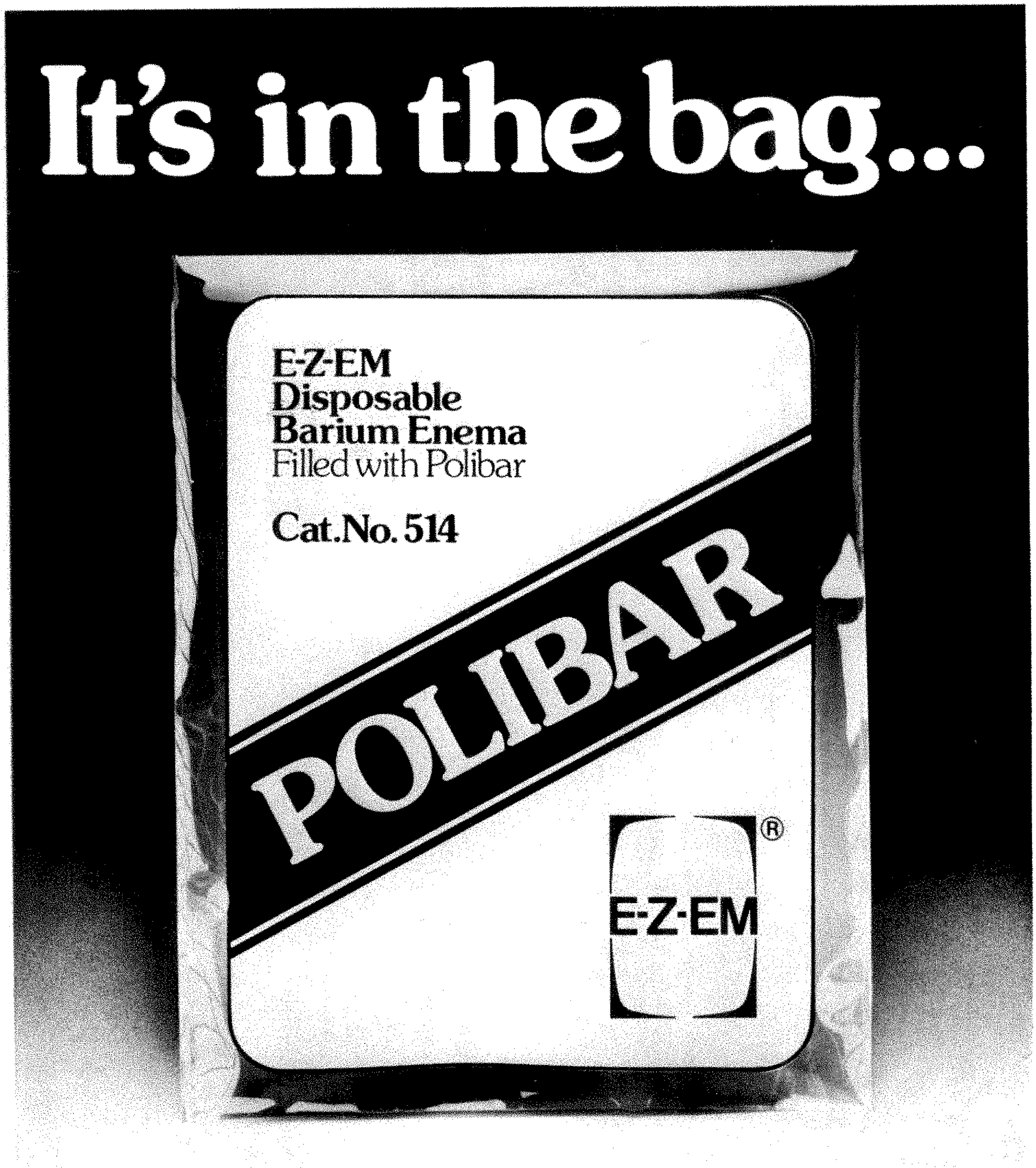
For details, speak to your Kodak representative.

He can give you up-to-date information on all areas of diagnostic imaging.

Kodak. We care about your image.

Kodak

KODAK 'Lanex' Regular Screens for special procedures are available to fit Puck, AOT and CGR rapid film changers. Kodak and all product names printed thus – 'X-Omat' – are trade marks.



E-Z-EM ®

The complete disposable barium enema kit.

Full details from:
Henleys Medical Supplies Ltd. London N8 0DL Tel: 01-889 3151

PL/1665/0001

Produced by E-Z-EM Ltd London

MAJOR NEW BOOK

Neuroradiology

● Scheduled for August publication.

E. H. Burrows and *Norman E. Leeds*

Two volumes 1184 pages 1573 illustrations hardback £90.00 approx ISBN 0 443 08016 X

This superb work provides a completely up-to-date and comprehensive text on the radiology of the brain and the spinal cord. It covers the most recently developed investigative techniques, with emphasis on non-invasive methods.
The second volume comprises a unique collection of 100 self-testing exercises, to enable the reader to consolidate the material in the first volume.

JUST PUBLISHED

A Textbook of Radiology and Imaging Edited by *David Sutton*

Third edition 2937 half-tone and 234 line illustrations
Single volume edition 1456 pages £65.00 ISBN 0 443 01700 X
Two Volume edition 698 and 800 pages £80.00 ISBN 0 443 02371 9

The standard work in the English language, completely revised and updated. The change in title reflects increasing emphasis on the new imaging modalities.

AVAILABLE NOW

Manual of Ultrasonography *Kenneth J. W. Taylor et al*

224 pages 253 half-tone and 128 line illustrations hardback £12.00 ISBN 0 443 08053 4

Indicates scanning techniques for demonstrating normal anatomy as well as pathology—for all who use ultrasound equipment.

Two-dimensional Echocardiography Edited by *Joseph A. Kisslo*

222 pages 158 illustrations hardback £11.00 ISBN 0 443 08076 3

This definitive new book emphasises the latest methods and focusses on their practical clinical applications in evaluation and management of patients.

Pearls in Diagnostic Radiology *Harold D. Rosenbaum*

240 pages 200 illustrations hardback £19.50 ISBN 0 443 08097 6

Provides case-orientated material which challenges readers to reach a correct diagnosis on the basis of the given radiological data, together with answers and discussion material.

New Techniques and Instrumentation in Ultrasonography

Edited by *P. N. T. Wells* and *Marvin C. Ziskin*

224 pages 152 illustrations hardback £12.00 ISBN 0 443 08075 5

A comprehensive survey of available techniques and instruments with direct relevance to clinicians using diagnostic ultrasound, including those likely to be more important in the future.

Ultrasound in Cancer Edited by *Barry B. Goldberg*

224 pages 80 illustrations hardback £12.95 ISBN 0 443 08144 1

Examines the ways in which ultrasound can be used to detect and identify tumours in specific areas of the body. Includes a chapter on the still-experimental use of ultrasound in therapy.

FORTHCOMING **Ultrasound in Emergency Medicine** *Taylor* and *Viscomi*

224 pages approx 271 half-tone and 17 line illustrations hardback £12.00 approx ISBN 0 443 08156 5

Churchill Livingstone

Robert Stevenson House, 1-3 Baxter's Place, Leith Walk, Edinburgh, EH1 3AF, U.K.

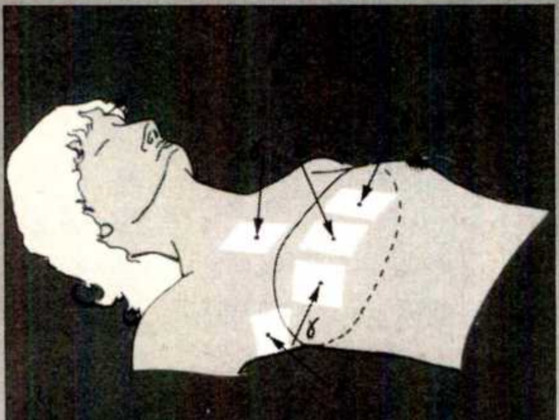
IT'S YOUR RESULTS THAT MATTER.

In planning and documenting radiation therapy.

The results of radiation therapy are inseparably linked to the precision and effectiveness of the treatment planning system. It is the crucial step between diagnosis and therapy.

The very best solution is the integration of CT-scanning results with three-dimensional treatment planning.

Therefore we have developed the new ONCOLOGY SUPPORT SYSTEM. It links up directly with any CT-scanner that produces data in standard format. The direct introduction of patient data, diagnostic results and tumour localization into an advanced treatment planning process offers great advantages to radiation therapy. In addition this system permits statistical evaluation of the recorded tumour data, applied doses and treatment technique as a basis for long-term department planning.



Three-dimensional planning

The ONCOLOGY SUPPORT SYSTEM can also be applied when patients have not been CT-scanned. In this case the patient data are entered graphically.

Ergonomic design of all system components permits easy efficient operation. Planning and evaluation procedures are facilitated by comprehensive software.

The new system is of course fully compatible with the VERICORD SYSTEM for Verification and Recording of treatment parameters.

To get full details about the ONCOLOGY SUPPORT SYSTEM and VERICORD SYSTEM please mail the coupon.

Philips Medical Systems cover the range of advanced diagnostic imaging and radiation therapy.

PHILIPS

Medical Systems

I want information about

○ ONCOLOGY SUPPORT SYSTEM ○ VERICORD SYSTEM

e

ital

et

o

ntry

Philips Industries
dical Systems Division-QM,
keting Communications
t, Eindhoven, the
Netherlands.
BJR

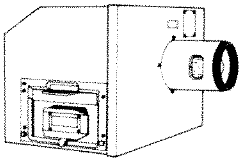
Oldelft offers you more than just a good camera... it gives you a complete system.

Oldelft makes high quality 100mm cameras for image intensifier photography and CRT display recording.
But that's not all. Oldelft also makes a whole range of products that simplify the entire film handling operation after exposure. Together, these products make up the Oldelft 100mm daylight system. It's based on the use of 10x10cm sheetfilm. But mainly it uses apparatus already available in radiological departments. Which means it fits smoothly into the department's work routine.
Nothing has to be changed.

Advantages of the 100mm sheetfilm system

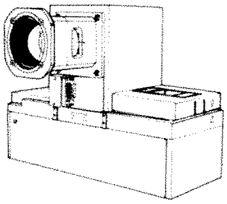
- the 100mm system works with sheetfilm - as you are used to in large-size radiography - which makes for easy sorting and selection and an efficient working routine.
- it works with medium-size film, which enables diagnostic information to be interpreted with the naked eye. It also cuts film and chemical costs and reduces x-ray dose for both patient and doctor.
- it works with the daylight magazine technique: its supply and take-up magazine hold enough film for a complete examination. No interruptions. No fussing with cassettes. Result: less time needed for examinations; better throughput of patients.
- the 100mm system is flexible. Components can be chosen to suit a hospital's individual needs.

General x-ray diagnosis



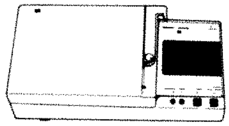
The Anodica-2 image intensifier camera is capable of up to two exposures per second. It is especially suitable for use in cases of gastro-enterology, neurology, urology, orthopaedics, gynaecology and paediatrics. Anodica techniques offset the disadvantages experienced with conventional large format radiography. Handling operations are considerably reduced and there is a marked increase in throughput of patients.

Special x-ray procedures

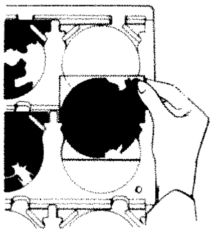


The high exposure rate of the Anodica HS - up to 12 exposures per second - offers great advantages in examinations such as general and selective angiography, cerebralangiography. Motion blur is reduced, focal spot of the x-ray tube is smaller and x-ray dose is low.
Use of Anodica exposure technique means that catheterization and image intensification can be simultaneous. It is therefore not necessary to move the patient.

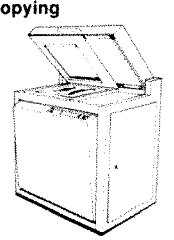
CRT display photography



With the Catodica camera-back for CRT display recording of ultrasound, gamma cameras and CT scanners, a substantially better quality image is obtained than is possible on positive paper film from instant camera-backs. The Catodica works with a magazine that can be loaded in full daylight.
The automatic film transport means great facility and quick examination.

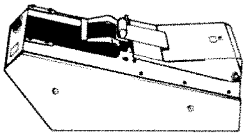


Film copying



The Delcomat provides a highly efficient copying service so that the exposures always remain at the radiological department. It gives top quality copies of large radiographs, complete or in part on 100mm sheetfilm.
It also duplicates 100mm exposures on 1:1 scale.
The Delcomat saves filing space and provides a basis for a teaching file.

Processing

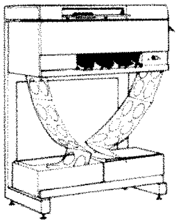


By means of the Film Feeder, 100mm sheetfilms can be processed automatically and in daylight, using normal large-size film processors without modification.
Small daylight processors for instant use with the camera are also available.

Viewing

For quick quality check and easy diagnosis, exposures can be mounted in correct order in the Cadrix, a simple plastic holder, which is placed on the viewing box. For large group discussion, as for example during teaching sessions, pictures can be enlarged through the Heliomat viewer or by means of an overhead projector.

Framing



The manually operated Delcadro offers a simple method of mounting six exposures together in an economical paper frame.
In this way pictures selected after viewing in the Cadrix can be kept together for orderly presentation and are readily filed. An automatic version of the Delcadro is also available. It is especially effective for handling large quantities of film.

In brief

The 100mm system offers an efficient method of picture registration for a large number of hospital examination areas.
It reduces cost, saves time.
For simple film handling, a sophisticated package of accessories is available.
And remember - 100mm film offers a basis for planning substantial reduction in filing space.

Please send me more information about the 100mm system.
I am particularly interested in:

☐ how to cut film costs	☐ 100mm spot film photography
☐ standardization on 10x10 film	☐ 100mm CRT photography
☐ filing space reduction	☐ 100mm copying services

Name ______________________

Address ______________________

City ______________________

Country ______________________

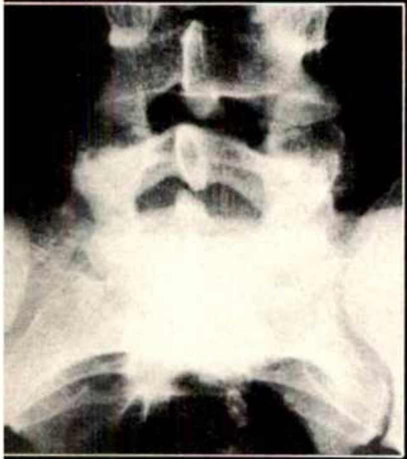
Oldelft nv Optische Industrie De Oude Delft

Holland, Postbox 72, 2600 MD Delft
Tel. (015) 14 59 49, telex 38011

U.S.A. Fairfax, Virginia 22030
2735 Dorr Avenue, Tel. (703) 573 7020, telex 089-2759

THE 3M TRIMAX SYSTEM:

THREE WAYS BETTER



. Finer diagnostic quality.

he gadolinium oxysulphide for-
ulation used exclusively by the 3M
rimax System ensures:
- a) better definition from this high efficiency phosphor
- b) less graininess from a finer, more regular grain structure
- c) better image characteristics by reduced probability of scatter.

2. Less exposure time.

The Trimax System is faster - up to 90% faster than conventional systems. This means:
- a) less radiation dosage,
- b) less chance of patient movement,
- c) greater use of fine focus.

3. Longer operating life.

Trimax screens, the first of which were introduced in 1974, have yet to show any loss of speed.

That's why they all come with an exclusive 7-year guarantee against loss of speed.

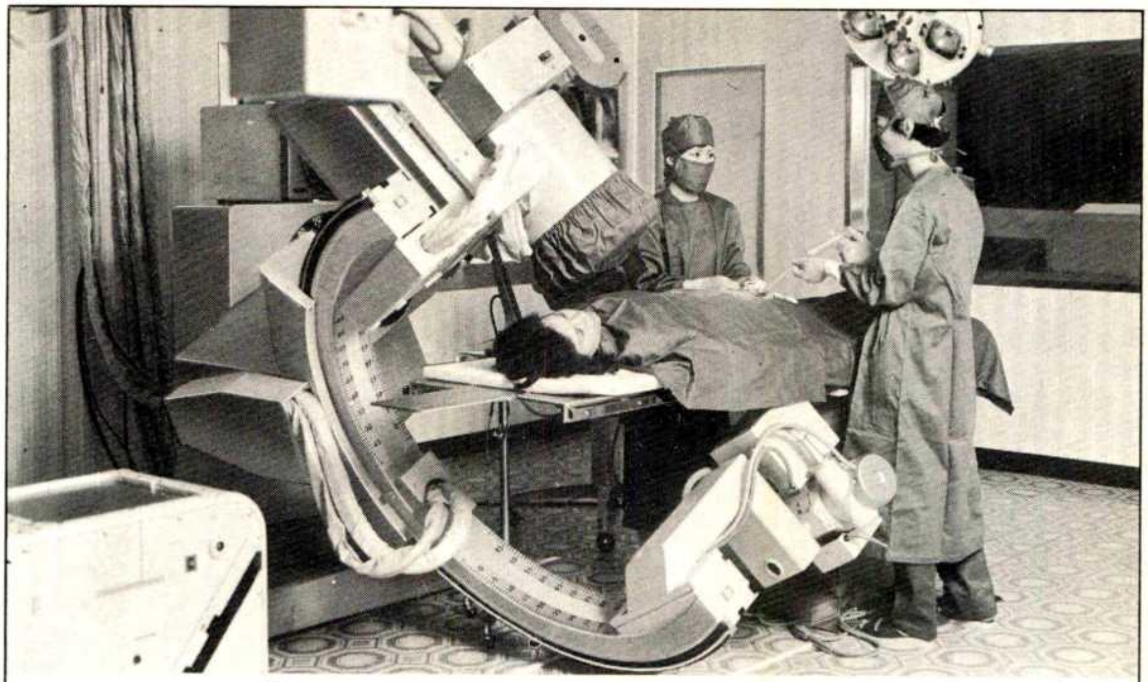
That's why replacement ceases to be a factor with the Trimax System.

When it comes to rare-earth x-ray systems,
here's only one which offers a fully comprehensive
ange of screens and films, designed to outperform
ll the others on the three most critical parameters
f: diagnostic quality, radiation dosage and
ng-term economy.

3M Trimax System. The most versatile, comprehensive and durable rare-earth system available. Specify it with confidence.

For further information about the Trimax System from 3M - the leaders in rare-earth phosphor technology - contact: Alan Budge, X-Ray Products, 3M United Kingdom Ltd, 3M House, PO Box 1, Bracknell, Berks, RG12 1JU. Telephone Bracknell (0344) 58458.

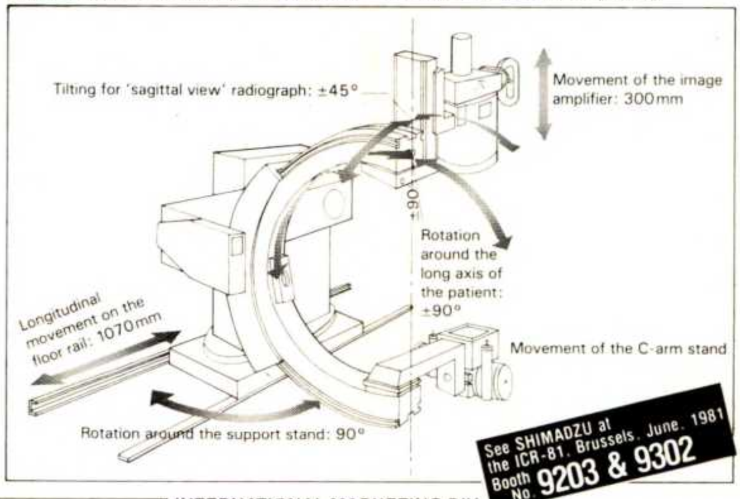
3M and Trimax are trade marks



New Shimadzu C.V.S. & Angiography System

The new, versatile MH-10 System is designed around a uniquely engineered "iso-centric" C-arm which provides a full range of three-dimensional movements.

Once set the unique C-arm system maintains a constant SID (Source-Image receptor Distance) that assures sharp multi-directional cinefluorographic and radiographic images. Additionally, the RF-30 Automatic Collimator can be used to keep the irradiation field a constant size even when changing the SID or viewing field of the image amplifier. This further permits effective fluoroscopy and cinefluorography at low X-ray dosages. Two OAT stands can be used; one for holding the film changer (up to 2X magnification) and the other to additionally hold the 2-directional X-ray assemblies (frontal and lateral). A PUCK film changer which provides up to 3X magnification can also be incorporated. Two kinds of catheterization tables can be chosen; the KS-40 which is just 5mm thick and highly impervious to X-rays, thereby producing radiographs of excellent contrasts, or the KS-40F frameless tabletop for fluoroscopy and cinefluorography.


Tilting for 'sagittal view' radiograph: ±45°
Movement of the image amplifier: 300mm
±90°
Rotation around the long axis of the patient: ±90°
Longitudinal movement on the floor rail: 1070mm
Movement of the C-arm stand
Rotation around the support stand: 90°

See SHIMADZU at the ICR-81, Brussels, June, 1981
Booth No. 9203 & 9302

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J
SHIMADZU (Europa) GmbH
4000 Dusseldorf 1, Johannes Weyer Str 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

tomatic, Computer-controlled Dynamic
d High Resolution Static B-scanning

e Sonography System RA-1 diagnostic ultra-sound
nner uses sophisticated, computer-controlled
ge processing to achieve superior image resolution.
e advanced, state-of-the-art scanheads comprise:
FOV scanheads for multiformat abdominal
nning.
V scanheads for high frame-rate scanning.
mall parts scanhead, incorporating Doppler with
ectral Analysis, for superficial vessel and organ studies,
neonatal and paediatric scanning.
e modular design guards against obsolescence whilst
mitting expansion and the ability to retrofit new
ging techniques as they are developed.

Universal Computer-controlled High Resolution Static B-scanning

The Universal Pho/sonic-SM fully-integrated computer-controlled, high performance ultrasound scanner which produces excellent image resolution. It is designed to meet individual requirements through a variety of system options, including:

- Wide range of transducers
- Image Process Functions
- Area, Circumference and Volume measurements.
- Obstetrics measurement facility
- Floppy disc interface

Future improvements to the image processing may be incorporated due to the flexible computer software.

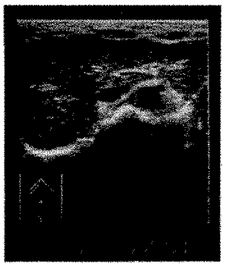
Other Siemens ultrasound equipment is available, including the IMAGER 2300, a Dynamically Focused Linear Array Real-Time B-scanner.
For full details write to: Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames, Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691.

..Siemens gives you the choice!

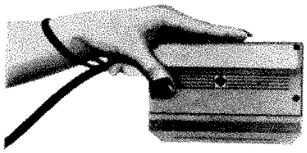
When you need to know the inside story, the Hitachi EUB-22 is a must.

More accurate clinical information is now available faster, thanks to Hitachi technology in this new real time ultrasound system.

The compact lightweight transducer provides access to all areas of interest making the TOMOSONIC EUB-22 ideal for abdominal, obstetric and neonatal imaging.

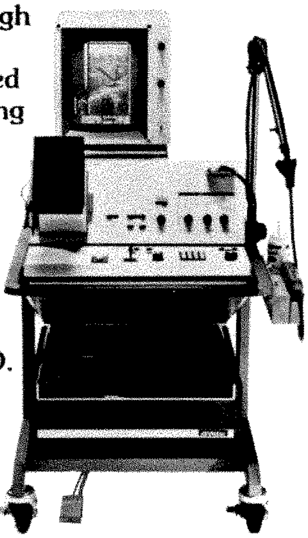


Dual image display allows expanded field of view or display of side-by-side images either in real time or freeze frame modes, with on-screen measurements.



Superb noise-free, high resolution images produced by advanced digital scan processing and transducer focussing techniques are displayed on the TV monitors. To facilitate the evaluation of those images the TOMOSONIC system provides an exclusive graphics display.

The patient's position during imaging is clearly displayed along with such valuable information as transducer position, patient I.D. date and gain.

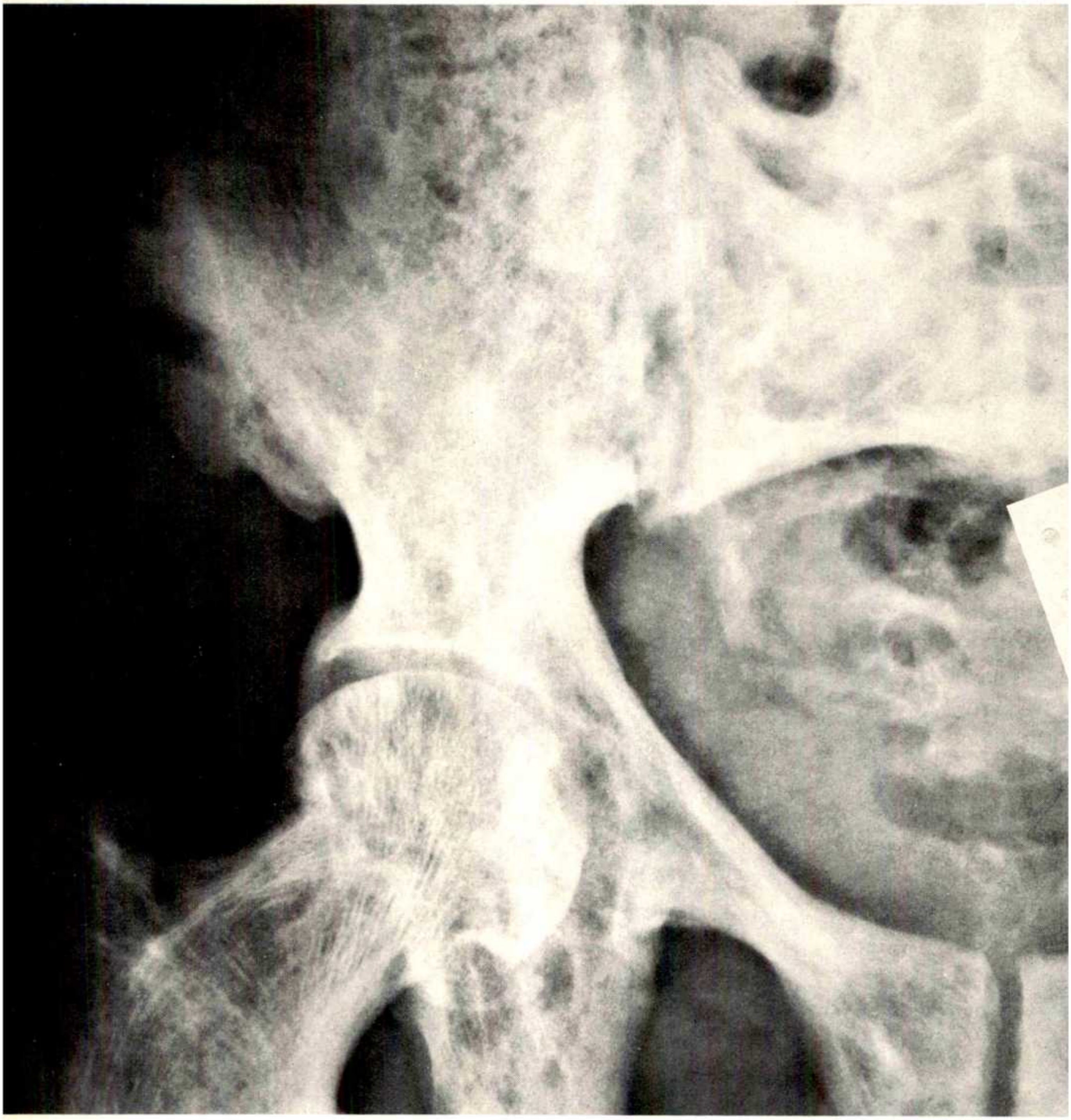


SONOTRON MEDICAL ELECTRONICS

SONOTRON LIMITED 29 MIDLAND ROAD, BEDFORD MK40 1PL ENGLAND TELEPHONE: BEDFORD (0234) 40881

also in: AUSTRIA-(02236) 86945 BELGIUM-(02) 7213424 GERMANY-(098) 3205051 FRANCE-(06) 9286945 SWEDEN-(040) 77585
or contact EUROPEAN HEADQUARTERS: SONOTRON AG NEUGASSE 247 P.O. BOX 353 CH 8031 ZURICH, SWITZERLAND TEL: 41-1-425841

The Oldelft 100mm system is

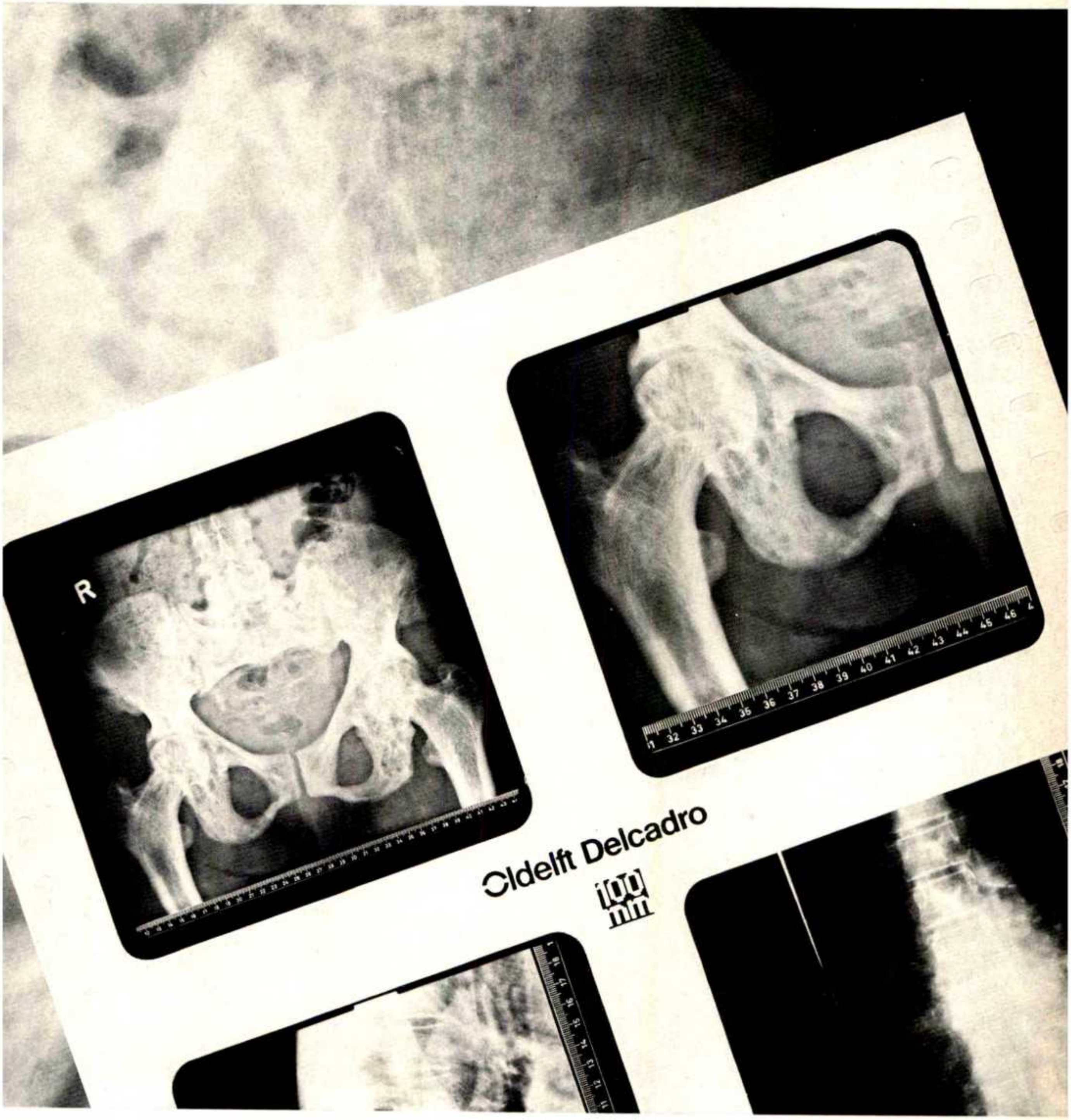


10x10 cm sheetfilm means substantial savings

Size- and cost-reduced copying with the Delcomat copier is another attractive feature of the Oldelft 100mm system that ensures optimum efficiency in your copying service. 100mm Delcomat copies of large-size radiographs and 100mm exposures have the full information content of the originals and can be used for the purpose of referral, interdepartmental information, teaching files, space-saving central files and lectures. They can be read without magnifying glass, their distribution is simple and postal costs are substantially reduced. 100mm Delcomat copies fit in with the ever increasing number of

delft products are sold by the
ading x-ray equipment manufacturers

more efficient and more economic



n copying costs

exposures made directly on 100mm sheetfilm with, for instance, the image intensifier cameras and CRT image recording cameraback of the Oldelft 100mm system. So this is an additional cost-saving aspect, because it means a better and more efficient use of the available peripheral 100mm equipment. The Oldelft 100mm system includes a wide range of accessories for the processing, framing and viewing of 100mm sheetfilm. They make for easy film handling and save time, money and space.

Oldelft: quality and reliability

Oldelft
nv Optische Industrie De Oude Delft

Holland, Postbox 72, 2600 MD Delft
Tel. (015) 14 59 49, telex 38011

U.S.A., Fairfax, Virginia 22030
2735 Dorr Avenue, Tel. (703) 573 7020, telex 089-27

Germany, Postbox 5420, D 6300
Giessen/Lahn, Tel. (0641) 4 10 49, telex 482930

Japan, Osaka, Postbox 1042.
Tel. (06) 309 09 61, telex 523 41 70

Sheffield Children's Hospital

PAEDIATRIC RADIOLOGY COURSE

16–19th September 1981

A course of lectures and film viewing sessions for consultants and senior registrars to equip them to deal with paediatric problems. Clinicians and radiologists will participate in sessions on gastroenterology, orthopaedics, urology, neurology and chest diseases. F.R.C.R. candidates welcome.

Further information can be obtained from
Dr. Steiner, Sheffield Children's Hospital
Tel. (0742) 71111.

Application forms and programmes from:
The Secretary,
Regional Postgraduate Committee,
Trent Regional Health Authority,
Fulwood House, Old Fulwood Road,
SHEFFIELD S10 3TH.

RADIOLOGY STUDY GUIDE

For passing radiology examinations

by KEITH SIMPKINS

Second edition 1981. A unique consumer's handbook for success in the FRCR II and other diagnostic radiology examinations. A goldmine of proven guidelines, packed with practical hints, recommended reading and key references.

Details from:–
Miss Margaret Johnston,
X-ray Department,
The General Infirmary at Leeds,
Great George Street,
Leeds LS1 3EX
(Tel: 0532 32799 Ext: 504)

Adelaide Children's Hospital Inc.

Paediatric Radiologist

Applications are invited from legally qualified medical practitioners for the position of Paediatric Radiologist at the above hospital. The successful applicant must be registrable as a specialist with the Medical Board of South Australia and would be responsible to the Director of Radiology for paediatric neuroradiology, computerised tomography and cranio-facial radiology. Duties will also include work in general paediatric radiology.

The department is new, having been recently re-equipped and performs approximately 30,000 paediatric radiology examinations per annum. Radiology, nuclear medicine and diagnostic ultrasound are incorporated into a division of organ imaging providing the latest diagnostic modalities. Computer tomography is provided through a CT 5005 scanner situated in an adjacent private hospital and all examinations are supervised by the Children's Hospital radiologist.

QUALIFICATIONS: Applicants should possess a higher degree in Radiology (M.R.A.C.R.) or equivalent. Experience and training in general paediatric radiology is required. It is desirable, although not essential, that the successful applicant have training and expertise in paediatric neuroradiology.

COMMENCING DATE: As soon as possible after appointment.

TERMS AND CONDITIONS OF APPOINTMENT: This is a permanent appointment and conditions are similar to those which exist in Government hospitals in South Australia. Conditions are covered in a document which is available on request. A limited right of private practice is permitted. Appropriate status may be arranged with the University of Adelaide.

SALARY RANGE: $A30,036 to $A40,204 p.a. Further details and particulars are available from the Director of Radiology.

Applications in writing, giving full personal and professional details, curriculum vitae, bibliography and the names and addresses of two referees close on 30th June, 1981 and should be addressed to the: **Medical Superintendent, Adelaide Children's Hospital Inc., 72 King William Road, NORTH ADELAIDE, S.A. 5006, Australia.**

Equals lowest noise

THOMSON-CSF's intensifier tubes for the 1980's feature increased X-ray absorption at the detector screen. This means better exploitation of the input information and less quantum noise in the output image.

... or lowest dose

These high-absorption intensifiers permit using appreciably reduced doses without any increase in output-image noise level.

... and equals enhanced images

The high spatial resolution and resolution uniformity of THOMSON-CSF's 4th generation technology, plus the reduced noise and increased contrast of the new high-efficiency screens, results in unequalled output image quality.

because as always,
THOMSON-CSF equals the highest available quality.

4358

THOMSON-CSF
COMPONENTS

THOMSON-CSF COMPONENTS AND MATERIALS Ltd / RINGWAY HOUSE / BELL ROAD / BASINGSTOKE RG24OQG
TEL.: (44.256) 29155 / TELEX: 858865

USA - Clifton NJ
THOMSON-CSF COMPONENTS CORPORATION
TEL.: (201) 7791004

BRAZIL - São-Paulo
THOMSON-CSF COMPONENTES DO BRASIL Ltda
TEL.: (11) 5424722

FRANCE - Boulogne-Billancourt
THOMSON-CSF DIVISION TUBES ELECTRONIQUES
TEL.: (1) 6048175

GERMANY - Munchen
THOMSON-CSF BAUELEMENTE GmbH
TEL.: (89) 751084

ITALY - Roma
THOMSON-CSF COMPONENTI
TEL.: (6) 6381458

SPAIN - Madrid
THOMSON-CSF COMPONENTES Y TUBOS S.A.
TEL.: (1) 4198842

SWEDEN - Stockholm
THOMSON-CSF KOMPONENTER
& ELEKTRONROR AB - TEL.: (8) 225815

JAPAN - Tokyo
THOMSON-CSF JAPAN K.K.
TEL.: (3) 2646346

ACTON TECHNICAL COLLEGE
RADIOGRAPHY EDUCATION COMMITTEE
present a Symposium

MORE FROM LESS

on 8th July 1981 at 9.00 a.m.
in Edward Lewis Lecture Theatre,
The Middlesex Hospital Medical School, London.

An exploration of the possibilities of obtaining more throughput from less resources. Topics to be explored include, manpower and its uses, equipment developments, film technology and politico/financial implications for medicine.

Refreshments, lunch and tea will be provided.

Further details from:
Symposium Secretary, Acton Technical College, High Street, Acton, London W3 6RD. Tel: 01–933 2344, ext. 2428, 2436.

HEINEMANN

Clark's Positioning in Radiography, 10th Edition

Volume 1 edited by Louis Kreel with the assistance of Ann Paris
Volume 2 edited by Louis Kreel

With the eagerly awaited publication of Volume 2 in April, this new and extensively revised 10th edition is now complete. The whole work has been largely rewritten in order to embrace the major and far-reaching recent developments in medical imaging. Radiographers must keep abreast of these and to this end new procedures have been considered in some detail, always with the emphasis on positioning where appropriate. However, the newest techniques are not routine everywhere and most of the basic special views are still needed : this edition affords them as much importance as ever.

Vol. 1 0 433 18832 4 483 pp/cased £22·50 net
Vol. 2 0 433 18833 2 916 pp/cased £22·50 net

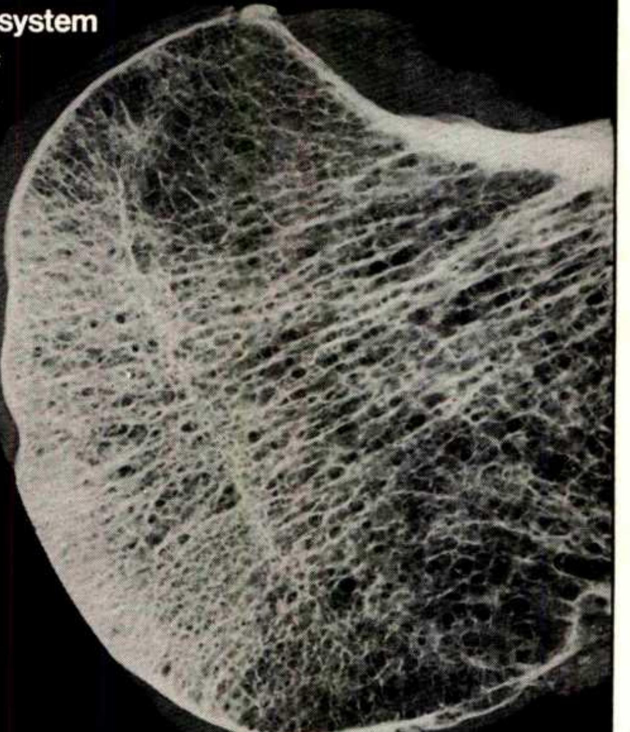
William Heinemann Medical Books Ltd
23 Bedford Square, London WC1 3HH

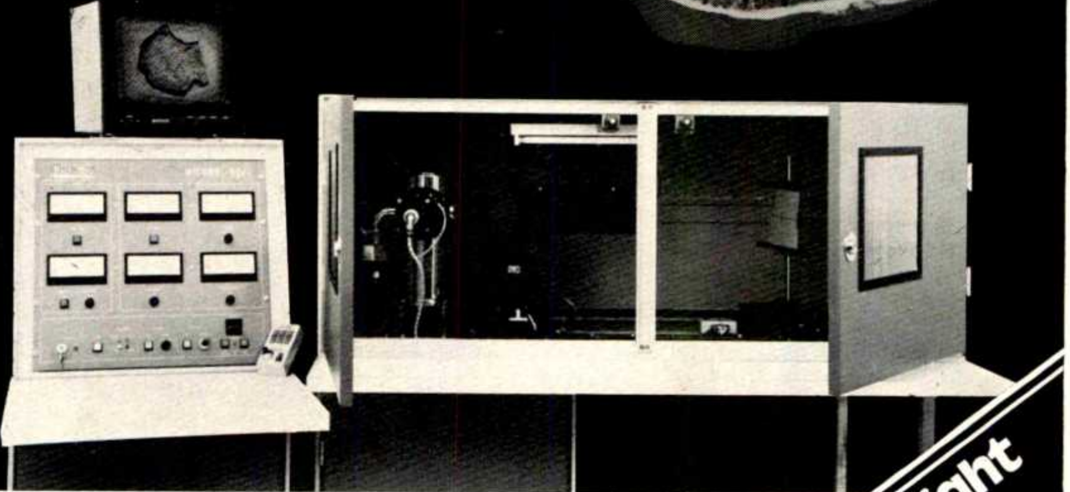
The new Nicolet Microx
Unique high definition Radiography

A completely united radiography system for imaging internal microscopic detail with infinite depth of field.

Discover the Microx difference

- High resolution 0·01mm
- Various magnification with zoom control of up to 25 times on film and 100 times on TV
- Thick sample capability
- No sample preparation
- Instant dynamic viewing on TV display
- Permanent high resolution photographic record with X-Ray or Polaroid film
- Stereo photography for three-dimensional viewing
- Large sample handling capacity
- Ample space for the addition of special sample handling devices
- Easy to use



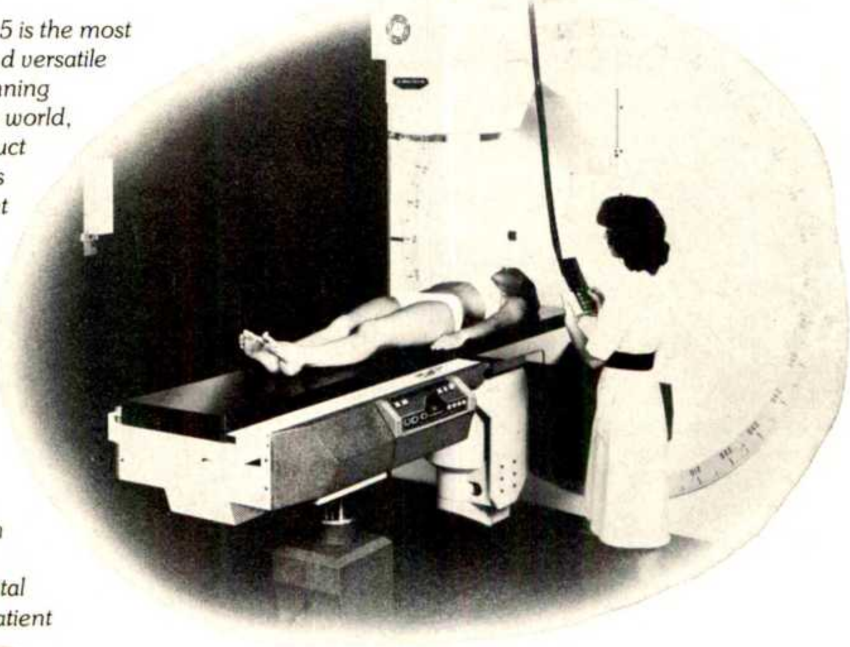


Nicolet Instruments Limited
A NICOLET INSTRUMENT SUBSIDIARY
Budbrooke Road, Warwick, England, CV34 5XH Tel: (0926) 44111 Telex: 311135

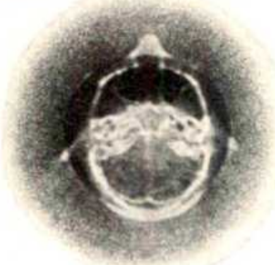
Get it right 1st time

Ximatron 5
Treatment Planning Simulator

The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.

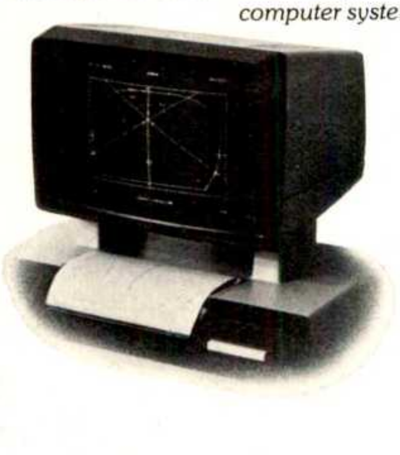


Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.

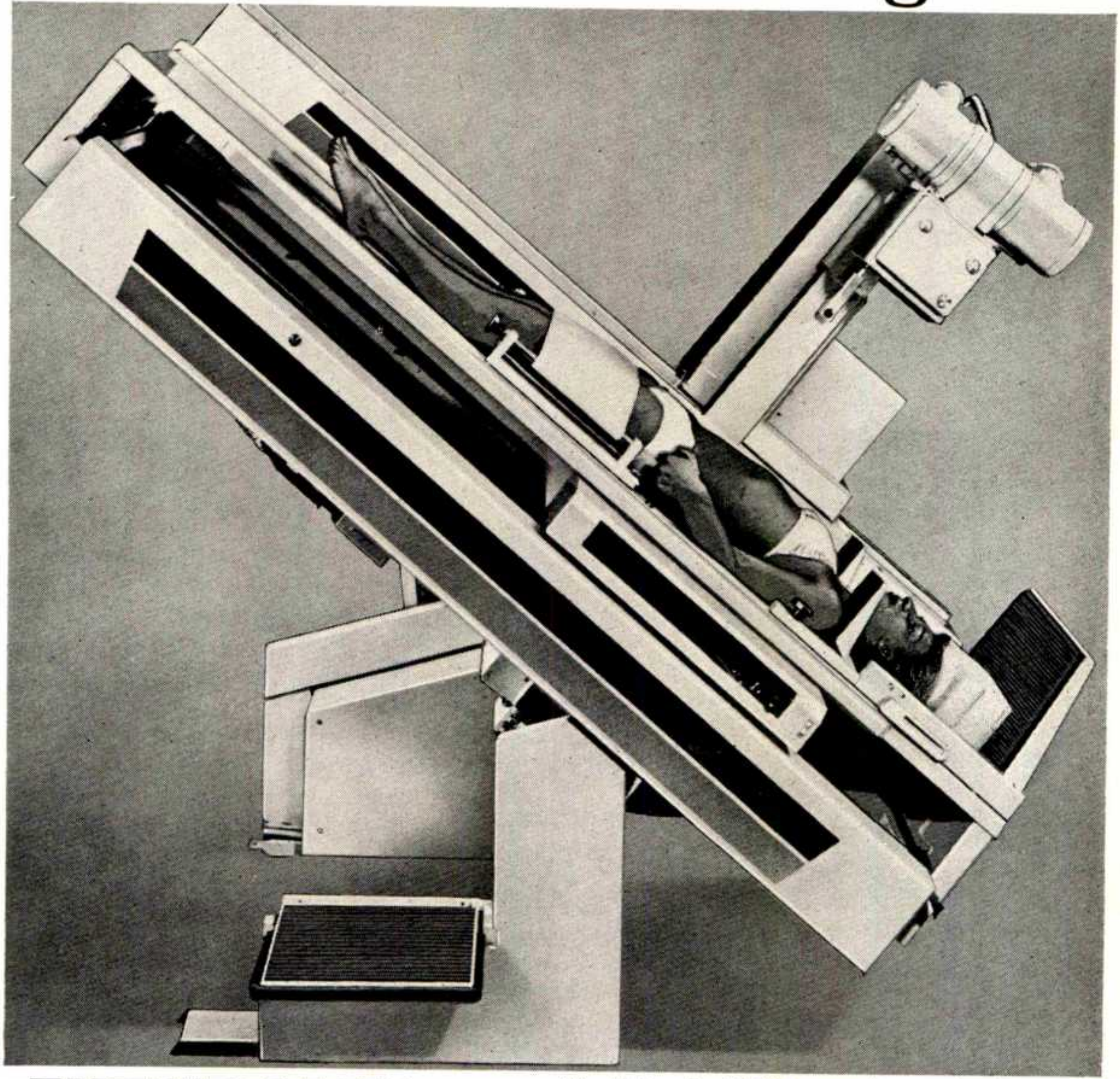
The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.



For further details:

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY

A remote controlled variable focus table with travelling tube



FUTURALIX
1600

CGR

Full details and specifications from
CGR Medical Limited
Astronaut House, Feltham, Middx. Tel: 01-890 8166

Branches at: *Bristol, Cambridge, Edinburgh, Glasgow, Manchester, Nottingham.*

The Futuralix 1600 is a new innovation in diagnostic X-ray with long-scan travel of the tube and image intensifier over 1600mm of the examination table. A D.C. motor achieves swifter, smoother speeds in impressive silence.

The Futuralix 1600 is unequalled for gastroenterology, urology, gynaecology and thoracic radiology and osseous studies.

The Futuralix 1600's electronically calculated parallel-plane tomographic movement also avoids parallex errors and achieves greater accuracy than mechanical systems. The movement of the spot device enables full myelographic examinations without the necessity for a 90°/90° table.

UNIVERSITY COLLEGE OF MEDICINE
LIBRARY

LET US SPELL IT OUT . . .

(FROM **A**USTRALIA TO **Z**AMBIA)

Australia, Austria, Bahrain, Bangladesh, Barbados, Belgium, Bermuda, Bolivia, Borneo, Brunei, Canada, Chile, Cyprus, Dominica, Dubai, Egypt, Falkland Islands, Fiji, Finland, Germany, Ghana, Gibraltar, Grenada, Guyana, Holland, Honduras, Hong Kong, Iceland, India, Iran, Jamaica, Jordan, Kenya, Kuwait, Malaysia, Maldives, Malta, Montserrat, Mauritius, Nepal, New Zealand, Nigeria, Norway, Qatar, St. Helena, St. Kitts-Nevis-Anguilla, St. Lucia, Saudi Arabia, Seychelles, Singapore, Switzerland, Tanzania, Trinidad, Yemen, Zambia.

Although we have *never advertised in any overseas journal* we find that we were in touch with all the territories listed above during 1980. We either helped with information about X-ray accessories or, more often, executed firm orders.

It is very gratifying to imagine that much of this originated with Radiologists and Radiographers who received their training in the United Kingdom. This would mean that they must have been sufficiently impressed by our reputation for "EVERYTHING X-RAY" to turn instinctively to us when problems arose after their return home.

It was in 1923, when we had only 13 years experience in this new-fangled X-ray business, that we first said . . .

Why not ask Andrews?

. . . and people are still doing it – all over the world!

CUTHBERT ANDREWS

EVERYTHING X-RAY LTD.

5 HIGH STREET, BUSHEY VILLAGE, WATFORD WD2 1BE

Overseas telegrams:
EXRAYZE WATFORD

Telephone:
01–950 2525

Telex:
Evex 925859 Elwood G

1981, *British Journal of Radiology*, 54, 443–466
VOLUME 54 NUMBER 642 JUNE 1981

The British Journal of Radiology

Review article

Heating techniques in hyperthermia

I. Introduction and assessment of techniques

By J. W. Hand, Ph.D.
MRC Cyclotron Unit, Hammersmith Hospital, Ducane Road, London W12 0HS
and Gail ter Haar, Ph.D.
Physics Division, Institute of Cancer Research, Sutton, Surrey SM2 5PX

(*Received June 1980 and in revised form December 1980*)

During the last decade there has been great interest in the use of hyperthermia in cancer therapy. The reasons why elevated temperatures, either alone or together with radiotherapy or chemotherapy, may prove useful have been the subjects of several recent reviews (Connor *et al.*, 1977; Field and Bleehen, 1979).*

Clinical applications of hyperthermia fall into two broad categories—whole-body and localized hyperthermia. During whole-body hyperthermia, which has been used on patients with advanced and widespread malignancies, core temperature is maintained at 41.8–42°C for a few hours. This appears to be the range of maximum tolerated temperatures; the organs which limit such treatment are the liver, which may be relatively sensitive to thermal damage, and the heart. Methods of inducing whole-body hyperthermia include the use of wax baths (Pettigrew *et al.*, 1974), hot air cabinets (Pomp, 1978), water blankets (Barlogie *et al.*, 1979) and space suits (Bull *et al.*, 1979). Common features of these methods are the reduction of heat losses from the patient and the introduction of thermal energy into the body to enable the desired level of hyperthermia to be reached rapidly. The heating techniques and associated monitoring of temperature are relatively simple and no further comment on them will be made here.

Local hyperthermia offers a wider range of therapeutic possibilities, especially if the temperature in a tumour can be maintained above that of surrounding normal tissue. The simplest method of heating is immersion in hot water. For man, treatment by this technique is restricted to the extremities. Although the temperature of the heating liquid is easily controlled, marked temperature gradients exist within the tissues and only the most superficial lesions may be treated. Similar problems and restrictions occur when body cavities such as the bladder (Ludgate *et al.*, 1978) are irrigated with hot liquids. Successful treatment of tumours of the extremities involving regional perfusion with preheated blood have been reported (Cavaliere *et al.*, 1967; Stehlin, 1969) but this method, too, is restricted to these anatomical sites.

The methods with greatest potential for inducing localized hyperthermia in patients are those involving electromagnetic waves (radiofrequencies and microwaves) or ultrasound. Much experimental and clinical work has involved techniques developed with the engineering and biological expertise gained from wide-ranging studies of the biological effects of non-ionizing electromagnetic waves. To date, the popularity of ultrasonically induced hyperthermia has not been so great, despite a number of advantages offered by this technique and the extensive experience with ultrasound in diagnostic medicine and physiotherapy. In Part I of this review of heating techniques we summarize the physical parameters and qualitative characteristics of methods currently available. Parts II and III are devoted to detailed discussions of the uses of non-ionizing electromagnetic waves and ultrasound respectively.

ASSESSMENT OF TECHNIQUES

Table I lists typical physical parameters for these modalities based on propagation of plane waves. The magnitude of the wavelength is an indication of the

---

*References to the literature will be found at the end of Part I on p. 446.

TABLE I

PHYSICAL PARAMETERS FOR ELECTROMAGNETIC AND ULTRASONIC HEATING OF TISSUES

	Electromagnetic waves			Ultrasound
	RF	Microwaves		
Frequency (MHz)	0.5→30	300→1000	>1000	0.5→5
Wavelength (cm)				
in muscle	610→61	11.9→ 4.1	1.8 (at 2450 MHz)	0.3→0.03
in fat	$\sim 2 \times 10^3 \rightarrow 218$	41→12.6	5.2 (at 2450 MHz)	0.3→0.03
in bone	$\sim 2 \times 10^3 \rightarrow 218$	41→12.6	5.2 (at 2450 MHz)	0.6→0.06
Penetration depth (cm)				
in muscle	130→14	3.9→ 2.4	1.7 (at 2450 MHz)	12→1.2
in fat	$\sim 10^3 \rightarrow 160$	32.1→14.3	11.2 (at 2450 MHz)	20→2.0
in bone	$\sim 10^3 \rightarrow 160$	32.1→14.3	11.2 (at 2450 MHz)	3→0.09*

*Data on ultrasonic attenuation coefficients in bone are sparse.

dimensions of the smallest volume that can be treated. The dimensions of the source of the waves relative to the wavelength determine the ability to produce a localized beam. In the case of MHz ultrasound, the short wavelengths involved permit well-defined beams to be produced. The interaction between waves and a target volume is determined by the relative magnitudes of the wavelength and the dimension of the target. In the case of microwave and ultrasonic radiation, these parameters are often similar. This leads to a complex interaction. The wavelengths associated with radiofrequencies (RF) are considerably greater than the dimensions of parts of the human body. In this case the electric and magnetic fields may be considered to be distributed as though they were stationary.

Penetration depth is defined as the depth at which the amplitude of a wave has decreased to e^{-1} of its value at the surface. It should be noted that at this depth the power density has decreased to e^{-2} (approximately 14%) of its value at the surface. The values listed are for plane-wave irradiation of semi-infinite slabs of tissue. They are only an indication of penetration for geometries of greater complexity. In the case of RF, penetration depths are of a qualitative nature since such distances have little practical meaning.

Characteristics of heating techniques currently available are listed in Table II. Focusing ability refers to the production of heating fields whose intensity is greatest at the target site. This may be achieved with a single applicator producing a convergent beam or with a multi-applicator array. With ultrasonic heating, focal volumes may be as small as a few cubic millimetres. In the case of a phased array of microwave or ultrasonic sources the focal volume would have dimensions of a few centimetres.

Localization of energy deposition is a function both of the geometry of the applicator or electrode and of frequency. In the case of microwave heating, a compromise between penetration and localization suggests the use of a frequency in the range 400–900 MHz. Ultrasonic hyperthermia offers advantages in localization as well as in focusing and in penetration.

Closely associated with the production of elevated temperatures are the problems of thermometry. Due to the strong dependence of the effects of hyperthermia on temperature, tissue temperatures should be recorded to 0.1°C. Ideally, thermometry in the presence of electromagnetic fields requires the use of small, non-metallic thermometers. A number of these non-perturbing probes have been developed and some are available commercially. In the case of ultrasound, temperatures may be monitored during insonation by means of fine thermocouples. The thermal properties of tissues must also be considered in the design of hyperthermal treatments; of particular importance are the vascularity and rate of perfusion with blood in tumours. These topics were the subject of a recent symposium (Jain and Gullino, 1980).

Capacitive coupling techniques at radiofrequencies offer the possibility of treating some deep tissue sites at the expense of localization, together with the risk of heating superficial tissues excessively. If an invasive method of heating can be tolerated, localized current fields (LCF) offer a relatively simple means of heating well-defined volumes of tissue. With RF induction coils, peak temperatures can occur at a

TABLE II

CHARACTERISTICS OF HEATING TECHNIQUES. THE SYMBOLS REFER TO THE QUALITATIVE ASSESSMENT OF A PARTICULAR CHARACTERISTIC

	RF				Microwaves		Ultrasound
Typical frequency range (MHz)	0.5–1		10–30		300–1000	>1000	0.5–5
Technique	RF heating of implants	Localized current fields	Capacitive coupling	Inductive coupling	Radiating sources, direct contact applicators, coaxial applicators.		Direct contact application, treatment through water bag.
Previous experience			Shortwave diathermy		Microwave diathermy at 433, 915, 2450 MHz.		Ultrasonic diathermy. Trackless lesioning.
Focusing ability	—	—	—	—	*	**	****
Localization	***	***	*	**	Radiating sources*, direct contact applicators**, coaxial applicators***		****
Thermometry	*	*	*	*	*	**	***
Advantages		1. Instrumentation relatively simple and inexpensive. 2. May be combined with techniques involving interstitial radioactive sources.	1. Ability to heat large volumes at depth.	1. In general superficial tissues heated less than deeper tissues.	1. Quite good penetration due to near field of radiating sources at 300–400 MHz. 2. Resonant absorption may occur at some sites. 3. Relatively small heating of fat. 4. Coaxial applicators useful for sites which are easily accessible through body cavities. 5. Development of systems involving microwave heating and microwave thermography. 6. Development of multi-applicator systems.		1. Good, flexible depth-dose relationship available with focusing. 2. Good penetration in soft tissues. 3. Possibility of enhancement of biological effects of temperature by non-thermal mechanisms. 4. Instrumentation available and inexpensive. 5. Development of system involving ultrasonic heating and ultrasonic imaging. 6. Technology available for multi-transducer systems and phased array.
Disadvantages	1. Requires expensive high power. 2. Difficulties in localizing implants.	2. Often invasive.	1. Excessive heating of superficial and fatty tissues.	1. In general heating patterns are non-uniform.	1. Heating patterns due to radiating sources difficult to predict. 2. Stray microwave radiation. 3. Large temperature gradients associated with coaxial applicators. 4. Poor penetration for frequencies greater than 1000 MHz.		1. Coupling medium required. 2. Large reflections at gas/tissue and bone/soft tissue interfaces. 3. Rapid attenuation in bone.
Contraindications	Presence of pacemakers				Presence of pacemakers.		Pregnancy.

— not applicable, * poor/difficult→**** very good/easy.

depth of several centimetres and the effective penetration of this method of heating compares favourably with those of microwave techniques.

Effective penetration of a few centimetres may be achieved with direct contact microwave applicators whilst coaxial devices may be used to treat sites which are accessible to catheters. The phenomenon of resonant absorption of microwaves may be used to produce differential heating in some sites. However, if deep tissue sites are to be heated effectively with microwaves, systems involving a number of microwave applicators must be developed.

The good penetration and short wavelength of ultrasound in soft tissues allow sharply defined regions of deep-seated tissues to be heated. An advantage of ultrasound over the non-ionizing electromagnetic radiations is that, by using focused beams, selective heating of deep tissue may be achieved. The main disadvantage of ultrasound is that its penetration in air and bone is very poor. The poor penetration in air results in a coupling medium being required between the source of ultrasound and the tissue to be heated. The volume of tissue that may be heated using a single, stationary ultrasonic transducer is less than that possible with other methods of local heating. However, larger volumes may be heated using either scanned transducers or multiple crossed-beam techniques. The imaging capabilities of diagnostic ultrasound may be used to advantage for tumour visualization before heating.

Clearly, no single method of inducing hyperthermia is applicable to all anatomical sites. Radiofrequency, microwave and ultrasonic methods need to be developed concurrently. Mathematical modelling which takes account of both physical and pertinent physiological parameters should prove valuable in determining optimum techniques. This, in turn, requires that the temperature dependence of physiological parameters such as blood flow should be known. Finally, the development of suitable thermometry and control instrumentation is necessary for the practical evaluation of each method.

REFERENCES

Barlogie, B., Corry, P. M., Yip, E., Lippman, L., Johnston, D. A., Khalil, K., Tenczynski, T. F., Reilly, E., Lawson, R., Dosik, G., Rigor, B., Hankenson, R., and Freireich, E. J., 1979. Total body hyperthermia with and without chemotherapy for advanced human neoplasms. *Cancer Research, 39,* 1481–1489.

Bull, J. M., Lees, D. E., Schuette, W. H., Whang-Peng, J., Smith, R., Bynum, G., Atkinson, E. R., Gottdiener, J. S., Grainick, H. R., Shawker, T. H., and DeVita, V. T., 1979. Whole body hyperthermia: a phase I trial of a potential adjuvant to chemotherapy. *Annals of Internal Medicine, 90,* 317–323.

Cavaliere, R., Ciocatta, E. C., Giovanella, B. C., Heidelberger, C., Johnson, R. O., Margottini, M., Mondovi, B., Moricca, G., and Rossi-Fanelli, A., 1967. Selective heat sensitivity of cancer cells. *Cancer, 20,* 1351–1381.

Connor, W. G., Gerner, E. W., Miller, R. C., and Boone, M. L. M., 1977. Prospects for hyperthermia in human cancer therapy—II. *Radiology, 123,* 497–503.

Field, S. B., and Bleehen, N. M., 1979. Hyperthermia in the treatment of cancer. *Cancer Treatment Reviews, 6,* 63–94.

Jain, R. K., and Gullino, P. M., 1980. Thermal characteristics of tumors. Applications in detection and treatment. *Annals of the New York Academy of Sciences, 335* (Proceedings of meeting in New York, March 1979).

Ludgate, C. M., Maclean, N., Pettigrew, R. T., and Tulloch, W. S., 1978. The effects of different methods of hyperthermic perfusion of the urinary bladder and the importance of neural tone. In *Cancer Therapy by Hyperthermia and Radiation,* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 328–330.

Pettigrew, R. T., Galt, J. M., Ludgate, C. M., Horn, D. B., and Smith, A. N., 1974. Circulatory and biochemical effects of whole body hyperthermia. *British Journal of Surgery, 61,* 727–730.

Pomp, H., 1978. Clinical application of hyperthermia in gynaecological malignant tumours. In *Cancer Therapy by Hyperthermia and Radiation.* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 326–327.

Stehlin, J. S., 1969. Hyperthermic perfusion with chemotherapy for cancers of the extremities. *Surgery Gynecology & Obstetrics, 129,* 305–308.

II. Non-ionizing electromagnetic waves

By J. W. Hand, Ph.D.

There is ample biological evidence that hyperthermia may be of use in the treatment of cancer. However, before clinical assessment of this treatment can be made, suitable techniques for heating tissues must be developed. The methods with greatest potential for inducing localized hyperthermia are those involving radio- and microwave-frequency electromagnetic waves or ultrasound.

In this paper the applications of non-ionizing electromagnetic waves are reviewed. Following a brief historical review, the radiofrequency methods of capacitive coupling, localized current fields, induction heating and heating of metallic implants are discussed. Microwave methods including direct contact applicators, coaxial applicators, radiating sources and multiple applicator systems are then considered. A brief discussion of the electrical properties of tissues is given in an appendix. Throughout the review the emphasis is either on direct clinical application or possible adaptation to the treatment of patients.

Closely associated with the production of elevated temperatures are the problems of thermometry. The use of conventional thermocouple and thermistor probes in the presence of electromagnetic fields can lead to perturbation of the heating fields, excessive heating of the probe and electronic interference. Since thermometry in hyperthermia is the subject of a recent review by Cetas and Connor (1978),* no further comment is made here except to stress that the development of thermometry is as important to the future of hyperthermia as the development of heating techniques.

Interaction of electromagnetic fields with tissues depends on their electrical properties. Most tissues may be broadly classed as being in one of two groups —those with high water content, *e.g.* skin, muscle, liver etc., and those with low water content, *e.g.* bone, fat. Firstly, movement of ions under the influence of the electric fields leads to ohmic heating; and secondly, thermal energy may be imparted to the medium through the interaction between rotating polar molecules and the alternating fields.

A brief summary of some of these interactions is given in Appendix 1. For extensive discussions of electromagnetic fields and biological materials the reader is referred to the works of Schwan (1957; 1959), and Grant *et al.* (1978). Extensive lists of the values of the dielectric parameters of a number of tissues over a wide range of frequencies can be found in Schwan (1957), Presman (1970), Tinga and Nelson (1973) and Durney *et al.* (1978).

The Use of Radiofrequencies

The use of high-frequency electric currents to heat tissues dates back to the end of the 19th century. The experiments of d'Arsonval between 1892 and 1898 had demonstrated the absence of neuromuscular response when currents with frequencies greater than 10 kHz were passed through the body. Shortly after this period von Zeynek observed tissue heating by high-frequency currents and, within a few years, radiofrequency energy became popular in the treatment of many conditions, using frequencies of the order of 1 MHz. Longwave diathermy, as it became known, required the use of electrodes which were in direct contact with the patient and the risk of burning superficial tissues was high. In the late 1920s Schliephake used currents of much higher frequency for clinical applications. This technique became known as short wave diathermy. An advantage of using frequencies of the order of tens of MHz was that electrodes no longer needed to be in contact with the skin since the capacitive reactance between an electrode and the tissue at these frequencies was sufficiently low. Shortly after this development Neymann investigated the use of electromagnetic induction for heating tissue. Detailed histories of these topics together with extensive lists of references have been given by Neymann (1938), Licht (1965) and Thom (1966).

At frequencies in the shortwave diathermy range the wavelengths are long compared with the dimensions of large experimental animals (*e.g.* dog, pig) and of parts of the human body (*e.g.*, at 27.12 MHz the wavelengths in air, fat and muscle-like tissue are approximately 11m, 2.4 m and 0.7 m respectively). The problem can therefore be treated as quasi stationary with the electric and magnetic fields assumed to be distributed in space as though they were static fields.

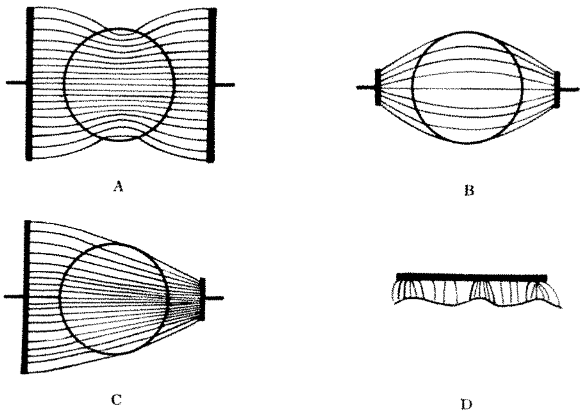


Fig. 1.

Schematic diagrams of electric fields for some arrangements of electrodes. Greater heating will occur in those regions in which the density of field lines is high.

(A) Relatively uniform heating will result when large electrodes are used at relatively large separations.

(B) When small electrodes are used there is a tendency for superficial regions to be selectively heated.

(C) When electrodes of different sizes are used there is increased heating under the smallest electrode. If one electrode is located closer to the tissues than the other, selective heating will occur under the closest electrode.

(D) If the separation between tissues and electrode is non-uniform local heating occurs at prominences due to a concentration of field lines.

---

*References to the literature will be found at the end of Part II, on p. 456.

*Capacitive coupling**

In the simplest form of this method the tissue to be heated is placed between, or near to, two electrodes which are connected to the output of a radiofrequency generator. It becomes an integral part of the output circuit of the generator. The electrodes may be rigid or flexible sheets of metal covered with suitable insulation. Figure 1 illustrates the dependence of the current distribution on the position and size of the electrodes relative to the tissue to be heated. When the electrodes are of equal area, the current density in the tissues adjacent to them will be the same. If electrodes of differing areas are employed, energy may be imparted to the tissues near the small electrode at a greater rate than to those near the large one. A problem with capacitive coupling is that if, for example, the spacing between electrode and skin is not uniform or if perspiration is present, the impedance will be non-uniform over the surface covered by the electrode. This leads to a non-uniform distribution of current and to "hot spots" where the current density is excessive.

Coulter and Osborne (1938) investigated the efficacy of several shortwave diathermy techniques by comparing the temperatures achieved in the quadriceps muscles in the thighs of human volunteers with those recorded in superficial tissues. They showed that both the types of electrode chosen and their positions with respect to the tissues were critical. More recently Guy *et al.* (1974) have discussed this technique and have drawn attention to a number of disadvantages. A considerably greater rate of rise in temperature is to be expected in the fat than in the underlying "wet" tissues because of a number of factors. For example, the dielectric constant ϵ and the conductivity σ of fat are small compared to those of skin, muscle etc.; the current density is greater in superficial tissues near to the electrodes than in deep tissues; and the specific heat of fat is lower than that of skin and muscle. An increase in relative heating at depth may be achieved by using electrodes of dimensions comparable with, or larger than, those of the tissues to be heated (Thom, 1966), by cooling the skin (Brezovich, 1979) or by using a "cross fire" technique (Scott, 1957).

Marmor *et al.* (1977) and Dickson *et al.* (1977a; b) used a 13.56 MHz generator with capacitive coupling to heat superficial tumours in rodents and rabbits. Although the factors discussed above limit the effectiveness of this method when heating large volumes of tissue at depth, the problems are reduced when relatively small, superficial volumes in animals with thin layers of fat are treated. In the studies in question heating was localized through the use of small electrodes around the tumours. Marmor *et al.* found that "relatively uniform" heating was achieved in tumours in the flanks of mice and that tumour temperature was usually about 0.5°C higher than that in surrounding normal muscle, although occasionally the muscle temperature was equal to or even higher than that of the tumour. On the other hand, Dickson and his co-workers, using somewhat larger tumours (less than 22 cm^3) on the legs of rats and rabbits, found that temperatures in tumour were significantly higher (3–4°C) than in normal muscle but measured variations of 2–3°C within the tumour. It was suggested that the temperature differences observed were a consequence of areas of relatively low blood flow in the tumours.

Using similar apparatus to that referred to in the previous paragraph, LeVeen *et al.* (1976) reported the heating of tumours in several sites in 21 patients as well as in experimental animals. Tumour temperatures in excess of 46°C, some 8–10°C higher than adjacent normal tissues, were recorded although the way in which the temperatures had been measured was not disclosed. Although these workers stated that "energy is best transmitted to a surgically exposed tumour in order to avoid undesirable heating of the skin and subcutaneous tissue", they failed to provide details of the heating procedures adopted.

Overgaard and Overgaard (1972) used 27.12 MHz shortwave diathermy with small insulated electrodes for local heating of mammary carcinomas (150–200 cm^3) implanted in the flanks of mice and drew attention to several factors which may lead to non uniform heating of such tumours. In a later publication, Overgaard (1978) investigated the local control of a number of different transplantable spontaneous mouse tumours following heating by the same method. The large number of recurrences recorded was probably due to the inhomogeneous heating of the tumours, especially around their periphery. Overgaard stated that greater uniformity in heating could be achieved by immersion in a water bath.

Localized current fields

Recently a new approach to radiofrequency heating has been attempted. Electrical currents of relatively low frequency (100 kHz–10 MHz) are passed through the treatment volume by means of electrodes which may be superficial and in direct contact with the skin, or interstitial, or a combination of these arrangements. The configuration and placement of the electrodes determines the pattern of energy deposition within the tissues. Since the electrodes are in contact with the tissues, there is no longer a requirement that the capacitive reactance between electrode and tissue be low. In fact, by operating at these relatively low frequencies, the currents flowing through the tissues are predominantly resistive in nature because of the high impedance presented to capacitive currents. Doss and McCabe (1976) refer to the technique as localized current fields (LCF) and discuss its application to a number of anatomical sites. For example, because of the difference in electrical conductivity between bone and bone marrow, localized heating of the marrow could be achieved by inserting electrodes into it. These authors also point out that it may be possible to heat the colon or oesophagus by inserting a cylindrical electrode into these organs whilst using a large external electrode around the trunk of the patient. Localized current fields can also be combined with interstitial radium treatments enabling the combined effects of heat and low dose rate radiations to be studied (Manning *et al.*, 1979).

---

*The term coupling is used to denote the transference of power between two circuit elements when these elements have capacitive or inductive reactance rather than a direct connection.

Some characteristics of the LCF technique have been described by Cetas and Connor (1978) who used interstitial electrodes in a number of configurations in either phantom models or dogs. The frequency of the heating currents was 500 kHz and the resulting temperature distributions were strongly dependent upon the positioning of the needle electrodes. The intensity of hot spots could be reduced by cooling the electrodes or by increasing the electrode contact area through the use of more needles. Astrahan *et al.* (1978), using phantom models, have investigated the improvement in temperature uniformity when the radiofrequency currents are switched between a number of sets of electrodes situated within and/or surrounding the region to be heated.

Day *et al.* (1976) have applied LCF to the treatment of spontaneous tumours in 18 cats and dogs. Hyperthermal treatments of 45°C for 30 minutes were administered with electrode configurations of two parallel rows of needles, 1–2 cm apart, or one large and one small surface electrode. Although tumours of the pharynx, tongue, vertebral column and eye region were successfully heated, their treatment proved more difficult than that of superficial tumours due to the problem of positioning of the electrodes.

Clinical applications of the LCF technique have been reported by Sternhagen *et al.* (1978). In two cases, lesions at the base of the tongue were heated using non-invasive electrodes whilst a rapidly growing mass on the floor of the mouth in a third patient was heated using two rows of interstitial needle electrodes. Non-invasive electrodes were also used to heat a supraclavicular mass (about 84 cm^3) and metastatic lesions in the region of a disarticulated hip stump.

Induction heating

An alternative method of using radiofrequency energy is that of induction heating. A coil carrying a radiofrequency current is placed around or near to the tissue to be heated. Since biological material is essentially non-magnetic, the time-varying magnetic field associated with the alternating current in the coil passes through the tissues unperturbed. This magnetic field induces an EMF which causes a current to flow in the tissues. Since the conductivities of tissues with high water content are greater than those of "dry" tissues, the magnitude of the induced current, and hence the rate at which energy is deposited, will be greater in wet tissues than in fat and bone. In this respect the induction technique offers a major advantage over the capacitive coupling techniques previously described.

Induction coils may be wound in the form of solenoids or as flat "pancake" coils. For any given tissue, the rate at which energy is deposited is proportional both to the frequency and to the square of the magnitude of the current in the coil. Frequencies in the range 10–30 MHz are commonly employed for induction heating. At frequencies lower than about 10 MHz the current necessary to induce sufficient heating in the tissues becomes impracticably large. At frequencies greater than about 30 MHz displacement currents between the turns of the coil and between the coil and the tissues result in greatly increased heating of superficial tissues. For this reason coils should be restricted to no more than 3–4 turns with adequate spacing between them. Sufficient spacing between coil and tissues is also necessary to avoid excessive heating of superficial tissue.

There have been a number of reports of heating deeply lying tissues by means of the induction technique. Coulter and Osborne (1938) showed that this method was more effective in heating the human thigh than any technique involving capacitive coupling. Kebbel *et al.* (1964) drew the same conclusion from a study in which phantoms were heated by a variety of techniques.

The choice of geometry of the induction coil is largely determined by the dimensions and location of the tissues to be heated. Flat "pancake" coils may be used when local heating is desirable. Figure 2A

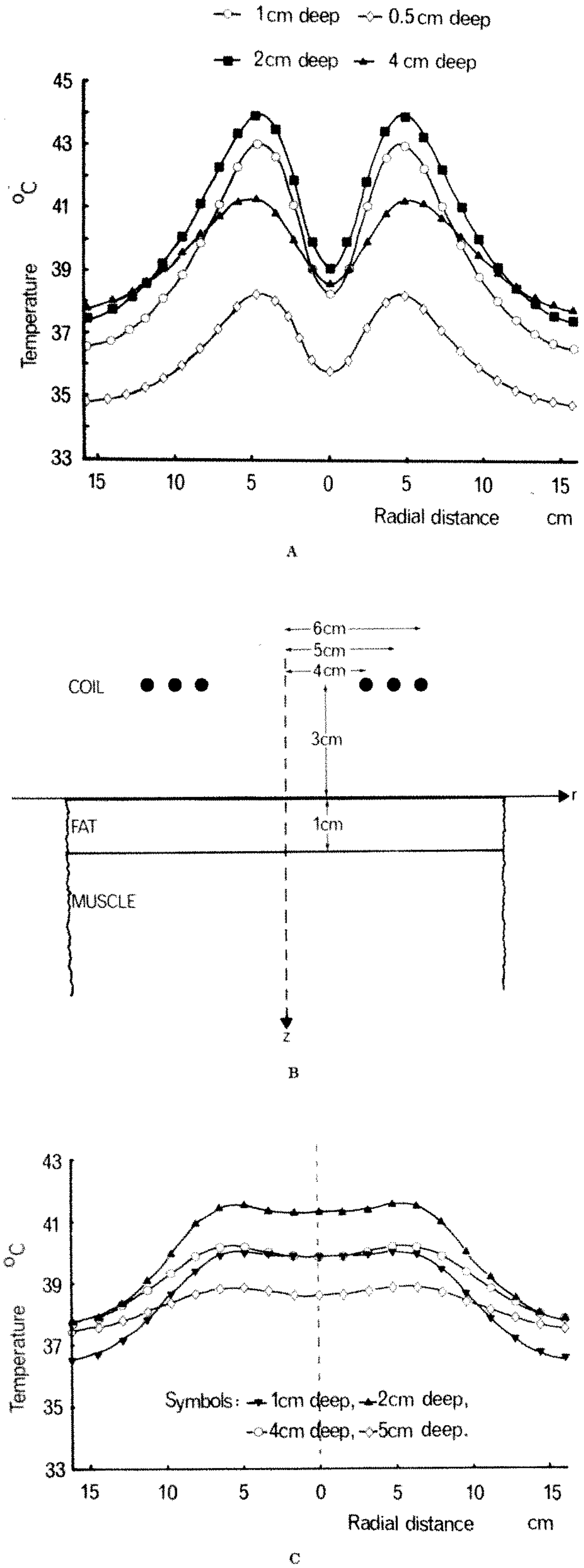


FIG. 2.

Steady state temperature distributions in a model of plane layers of fat and muscle tissues produced by a plane, three-turn coil (radii 4, 5 and 6 cm) carrying a 27.12 MHz alternating current. The thickness of fat is 1 cm and the separation between tissue surface and coil is 3 cm. The observed power density is calculated analytically; the resulting temperature distributions are computed using a finite difference method (Hand *et al.*, 1980). The effects of blood flow and thermal diffusion are taken into account in the model. (A) Stationary coil; (B) The geometry of the model; (C) Coil scanned at constant speed with an amplitude of ±6 cm.

shows the temperature distribution found by a mathematical model of heating due to a pancake coil of three turns placed above plane layers of fat and muscle-like tissues with the geometry shown in Fig. 2B. The penetration depth (the distance into muscle in which the absorbed power density is reduced by a factor $1/e^2$) is approximately 4 cm. By scanning the coils over a tissue the radial variation in these patterns can be reduced (von Ardenne, 1978). The heating pattern associated with this technique is shown in Fig. 2C. Improved uniformity in heating at depth may be achieved by using a pair of pancake coils placed on either side of the tissues and connected in series (Merriman *et al.*, 1934).

Shingleton *et al.* (1962) studied local tissue heating and the effect of tissue temperature on the uptake of an alkylating agent. The hind limbs of hypothermic (32°C) dogs were heated to 42°C by placing them between a pair of coils carrying 27 MHz current. Heating rates of 0.3–0.5°C per minute were achieved within the limbs without burning superficial tissues when the coils were suitably spaced from the skin. In another publication (Bryan and Shingleton, 1963) these workers give details of a number of pancake coils in addition to discussing systems consisting of both flat coils and solenoids.

More recently Kim *et al.* (1977) and Antich *et al.* (1978) have employed induction heating in the treatment of patients with malignant cutaneous lesions. A three-turn coil of outer radius approximately 5 cm was used at a frequency of 27.12 MHz to raise skin surface temperature to 43.5°C. In a study of thermal dosimetry with this RF method, temperatures in normal tissue and in tumours were recorded whilst keeping RF power and the position of the coil constant. Distributions of the maximum temperatures achieved and of times taken to reach these temperatures were approximately Gaussian in the case of normal tissue. For tumours, the distributions were broader and exhibited tails representing higher temperatures and longer times.

When larger volumes of tissues are to be heated, for example during whole-body hyperthermia, coils with approximately rectangular geometry may prove useful. Bigelow *et al.* (1952) used such coils to resuscitate dogs and monkeys from severe hypothermia. Single-turn coils 8–13 cm wide and 36–46 cm long were found to be satisfactory for treating dogs (6–14 kg), whilst smaller, one-and-a-half turn coils were necessary for efficient transfer of energy to small monkeys. These authors, too, stressed that the positioning of the animal between the coils was important both in regard to the rate of rewarming and to the incidence of burns. Although initial experiments were carried out at 13.56 and 27.12 MHz, the former frequency was chosen for later experiments solely because of reduced capacitive leakage between coils.

Radiofrequency heating of metallic implants

Localized heating of tissues may be achieved by implanting metallic materials into the region of interest and subjecting them to an external RF electromagnetic field. An early report of this technique was that of Medal *et al.* (1959), who injected suspensions of Fe_2O_3 particles, 0.02–0.1 μm in diameter, into the lymphatic systems of rats and rabbits. The animals were placed within helical coils connected to a high-power RF generator (120 kHz, 14 kW). Use of this relatively low frequency caused little heating of the undoped tissue whilst the iron oxide particles were heated as a result of hysteresis effects.

In considering the application of the technique to brain tumours, Moidel *et al.* (1976) suggested that small pieces of metal might be stereotactically implanted in a tumour. These authors investigated the relative heating rates of several implant materials and succeeded in producing controlled, localized hyperthermia in a frontal lobe of a live monkey brain.

A related method was used by Burton *et al.* (1971) to coagulate brain tissue. In an attempt to avoid the elaborate procedures necessary to achieve predictable and repeatable temperatures when using implants these authors took advantage of the fact that, under certain conditions, the heating rate of an implant is particularly dependent upon magnetic permeability. "Thermoseeds" which became non-magnetic at the high temperatures consistent with tissue coagulation were developed. It may, however, be possible to develop alloys with Curie points* in a range more suitable for hyperthermal treatments. The inherent temperature regulation of such an implant would be a very attractive feature.

Although implant techniques offer selective heating of local regions, they have a number of disadvantages. Any implant used must be biologically inert and, in order to achieve uniform localized heating, doping must be uniform and restricted to the tissues to be heated. In addition, expensive RF generators are needed to provide the necessarily high power levels.

THE USE OF MICROWAVES

Microwave radiation is the term applied to that part of the electromagnetic spectrum between 300 MHz and 300 GHz. However, since microwaves of frequency greater than about 10 GHz are absorbed within the most superficial layers of tissue, only frequencies lower than this are of interest in hyperthermia research.

An early, anecdotal report on the use of relatively low frequency (400 MHz) microwaves in cancer therapy was that of Denier (1936). In addition to reporting numerous animal experiments, he described the treatment of seven patients with microwaves alone or together with radiotherapy. However, it was not until after World War II, when GHz microwave sources of sufficiently high power became available, that investigations into the therapeutic application of relatively high-frequency microwaves could be made (*e.g.* Krusen *et al.*, 1947). Shortly afterwards the frequency of 2.45 GHz was formally allocated to industrial, scientific and medical (ISM) purposes. Schwan and Li (1955; 1956) suggested, on theoretical grounds, that such a choice of frequency was far from optimum if microwave radiation was to induce predictable deep heating in humans. They pointed out that the use of frequencies lower than 1 GHz would result in greater penetration into tissues and, because of the greater wavelength of these radiations, the heating of superficial layers would be less dependent on the thickness of skin and subcutaneous fat. These predictions were confirmed by Lehmann *et al.* (1962; 1965). General acceptance of the advantages of using lower frequencies led to the allocation of 915 MHz as an ISM frequency. In some countries, for example Germany (but not the UK or USA), the use of 434 MHz was authorized.

A simple technique, often used with conventional microwave diathermy machines, is to irradiate tissue in air from an antenna or microwave horn. However, subsequent absorption of microwaves may be difficult to predict and inadequate uniformity of temperature may result.

---

*All ferromagnetic materials become non-magnetic when heated to a sufficiently high temperature. This temperature is known as the Curie point of the material.

The electric and magnetic fields associated with a microwave source are dependent upon distance from the source. Far from the source the E- and H-fields are inversely proportional to distance and are orthogonal to each other and to the direction of propagation of the wave. The region in which these conditions holds is known as the "far field". At points near to the source the E- and H-fields are more variable and their relationship is more complicated. An absorbing body placed in this "near field" may interact with the source and affect the power radiated by it. For these reasons it is advantageous to perform irradiations in the far field of a microwave source. The boundary between near and far field regions occurs at approximately $2D^2/\lambda$ from the source where D is the largest dimension of the source and λ is the wavelength of the radiation. However, radiating devices at 915 and 434 MHz become impracticably large when they are used under far field conditions and localization of heating becomes difficult. To overcome these problems direct contact applicators have been developed.

Direct contact applicators

Direct contact applicators are generally sections of wave-guide or microwave cavities placed in direct contact with the tissue to be heated. These applicators have a number of advantages. For example, since the electromagnetic fields are limited to the areas of tissues treated, efficient use of the microwave energy can be achieved and only moderate power levels (less than 100 W) are required. In addition, stray radiation is at a low level (Kantor, 1977; Lehmann *et al.*, 1979) and measurement of the energy imparted to the treated area is a relatively simple task.

A tuned cavity applicator was tested by Lehmann *et al.* (1970). This had a 12×15 cm aperture and, by suitable loading with dielectric materials, could be operated at either 915 or 750 MHz (a frequency previously suggested as an optimum diathermy frequency (Guy and Lehmann, 1966)). An additional feature of this device was a facility for cooling the surface of the tissue beneath the aperture and thus avoiding overheating the most superficial tissues. Heating patterns produced in phantoms at these two frequencies indicated that differences between them were too small to be of practical significance. Delateur *et al.* (1970) used the 915 MHz applicator to heat the anterior thigh in human volunteers and achieved muscle temperatures in the range 40°C–42°C without exceeding tolerance levels in the subcutaneous fat.

The effects of varying the size of the aperture and the operating frequency on heating patterns produced in a plane slab model were studied by Guy (1971a). He predicted that an applicator of rectangular cross section and operated in a TE_{10} mode would achieve a ratio of deep to superficial heating significantly greater than that produced by plane-wave irradiation if the aperture was one wavelength high and between one and two wavelengths wide. Predominant superficial heating could be expected with small apertures whilst large apertures produced heating patterns of greater complication. These predictions were verified by thermographic studies on phantom models (Guy, 1971b). Following these studies, Guy *et al.* (1978) have developed a 915 MHz direct contact applicator. The device, constructed from two separate waveguides, has an aperture 13×13 cm and is loaded with a lightweight foam dielectric. Chilled air may be blown through the aperture onto the surface of the tissue to eliminate undesirable surface heating. Experimental and numerical studies of the effects of surface cooling with this applicator have been described by Emery *et al.* (1979) whilst experiments carried out on human volunteers by Lehmann *et al.* (1978) showed that temperatures at 1–2 cm in muscle could be elevated to 43–45°C.

Since microwave absorption is influenced by tissue geometry, analyses of heating patterns based on models with plane geometry are valid only when the curvature of the tissues under the applicator is large compared to the dimensions of the aperture. The effects of tissue size and curvature on absorption characteristics when applicators are in direct contact with cylindrical and spherical models have been investigated by Ho (1971; Ho *et al.*, 1979). Studies using phantom models of human limbs indicated that the minimum relative heating in the fat region occurred when the height of the aperture was equal to one wavelength in the fat and that curvature of the tissues could lead to standing wave patterns in the muscle region. This was particularly marked when the thickness of the muscle layer was equal to about half a wavelength. Under these conditions appreciable heating of deep tissues may be achieved. In the case of spherical phantom models the use of applicators with large apertures is suggested if heating at depth is desired. For any given sphere, the effective penetration of microwaves exhibits a resonant dependence on source frequency. The resonance frequency increases as the size of the sphere decreases. For small spheres (radius of muscle region less than 5–6 cm), the maximum heating may occur within the sphere rather than in a superficial region.

The resonant absorption of microwaves by mammalian cranial structures can lead to differential heating of the brain; such a method of heating might prove a useful adjuvant to chemotherapy or radiotherapy in the treatment of brain tumours. Irradiation at 2450 MHz can produce selective heating at the centre of a brain of diameter 6 cm (that of a cat or dog) but only superficial heating in a human brain (diameter approximately 14 cm). However, if irradiation is at 915 MHz, selective heating near the centres of both brains may be achieved.

Lin *et al.* (1973) measured temperatures in the brains of cats exposed to 915 MHz microwaves from a cavity radiator. Differential heating of the brain was observed and internal peak temperatures of 43°C were easily attained. Michaelson *et al.* (1979) used 2450 MHz contact applicators to raise the temperature in the brains of dogs to 39–42°C for periods of one hour and showed that the uptake of a radioactive tracer in the brain increased at high microwave power levels. The authors suggest that this method of localized hyperthermia could enhance the ability of chemotherapeutic agents to cross the blood-brain barrier.

Another factor which must be considered in the design of a direct contact applicator is the electric field distribution in the plane of the aperture. For applicators of rectangular cross section excited in the TE_{10} mode, the electric field distribution displays a maximum at the centre of the long wall, whilst it is uniform in the direction parallel to the short wall. This is shown in Fig. 3A. Since uniform heating is advantageous in many applications, a number of applicators with more uniform electric field distributions have been developed. Symmetrical heating profiles have been achieved by using applicators with circular polarization (Kantor *et al.*, 1978). Rectangular waveguides partially loaded with dielectric slabs can provide improved heating patterns (Van Koughnett and Wyslouzil, 1972; Kantor, 1977; Cheung *et al.*, 1977). Stuchly and Stuchly (1978) describe applicators which are excited in two modes (TE_{10} and TE_{30} (see Fig. 3B)) with orthogonal polarizations, whilst a versatile multimode applicator has been discussed by Lin and Kantor (1978). This consists of three concentric circular cylinders; either coolant to protect superficial tissues, or ionizing radiation for combined hyperthermia and radiotherapy, may be introduced into the inner cylinder. The inner and middle, and middle and outer, cylinders define coaxial waveguides which can support TE_{11} and TE_{21} modes (see Fig. 3C) at a single frequency or TE_{11} modes at two different frequencies. These combinations achieve heating patterns with circular symmetry and good uniformity.

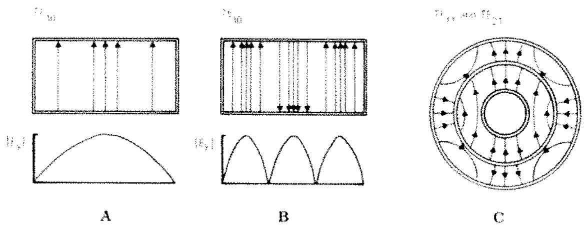


FIG. 3.

Instantaneous electric fields in a cross section of a rectangular waveguide carrying (A) a TE_{10} mode and (B) a TE_{30} mode. The lower diagrams illustrate the magnitude of the electric field as a function of position across the wide wall of the guide. (C) Instantaneous electric fields in a cross section of coaxial waveguides carrying a TE_{11} mode (inner–middle cylinders) and a TE_{21} mode (middle–outer cylinders).

Many of the problems of microwave-induced hyperthermia have been experienced in experiments involving animals; the understanding gained from their solutions has been valuable to the development of heating techniques for clinical use. For example, even when treatments are carried out in the far field of a microwave source the prediction of heating patterns remains difficult since changes in shape, size and orientation of exposed animals alter the absorbed energy and its distribution within the animal (Szmigielski, 1976; Hand, 1977). Cheung *et al.* (1978) achieved efficient microwave coupling to small tumours by encapsulting them in spherical expanded polystyrene moulds containing tissue-equivalent phantom material (Guy, 1971b). The size of the spheres (4–5 cm diameter) was chosen so that resonant absorption occurred and the tumours were located within the spheres in a region where heating was relatively uniform. Improvement in temperature uniformity resulted from the thermal insulation afforded by the expanded polystyrene moulds.

In general, waveguide applicators are loaded with material of relatively high dielectric constant if they are to be of a practical size to treat experimental animals (Mendecki *et al.*, 1978; Magin and Kantor, 1977). Magin (1979) has described a four-channel heating system in which animal tumours are bolused by a semi-solid gel and heated by small, 2450 MHz waveguide applicators. However, the experiments of Robinson *et al.* (1978) illustrated that improved temperature distributions could be achieved in microwave-heated mouse tumours if a liquid bolus was used. This consisted of 20% ethanol in isotonic saline (Cheung and Harrison, 1978) and was maintained at a temperature close to that desired within the tumour to minimize intratumour temperature gradients. A physiologically compatible liquid bolus has been developed and used in a similar way to enable sensitive normal tissues to be heated uniformly (Hand *et al.*, 1979a).

Co-axial applicators

A direct contact applicator can be operated only within a relatively narrow band of frequencies and, if it is to produce its optimum heating pattern at a particular site, should be designed for that particular purpose. However, microwaves can also be propagated along coaxial lines. Unlike waveguides, coaxial lines do not have a low frequency cut-off and can be used over a wide range of frequencies. Semi-rigid coaxial cables are available commercially in a number of sizes with diameters as small as 200 μm. Such cables can be inserted easily into tissues, either as interstitial implants or via a catheter into a body cavity.

Implantable coaxial applicators have been developed by Taylor (1978a; 1978b) and Szwarnowski *et al.* (1980). Heating may be produced with low levels of microwave power (less than 10 W) directly at the site of interest without affecting overlying tissues. The broad-band nature of such devices enables the size of the approximately ellipsoidal heated volume to be varied by changing the microwave frequency. However, when operated at 2450 MHz, these applicators produced marked temperature gradients (2–4°C per cm) in both phantom materials and tissues. Le Bourgeois *et al.* (1978) have shown that improved heating patterns may be produced by an array of coaxial applicators. These authors also suggest that the coaxial applicator could act as the antenna of a microwave radiometer to detect the black-body radiation emitted by the heated volume of tissue. By switching between heating and detection modes, a heating system inherently capable of measuring temperature could be developed. A number of coaxial applicators designed for particular applications have been described. For example, Bigu del Blanco and Romero-Sierra (1977) have used a hypodermic applicator which permits injection of a chemical into the tissue during heating, whilst Mendecki *et al.* (1978) have discussed applicators designed to be inserted via catheters into body cavities. The heating characteristics of these devices could be given a directional dependence by the addition of a reflector near the radiating element.

Taylor (1978a) has described an applicator which can be inserted through a stomach tube and used to produce localized hyperthermia in the oesophagus or other regions accessible through stomach tubes. An array of radiating elements is formed by joining inner and outer conductors at points spaced by half a wavelength along a flexible coaxial cable 2.65 mm in diameter. A uniform cylindrical heating pattern can be achieved by mechanical motion or frequency sweeping.

434 MHz radiation sources

The use of 434 MHz microwaves is sanctioned for medical purposes in some European countries (*e.g.* Germany) and a number of diathermy machines operating at this frequency are available commercially. Kebbel *et al.* (1964) have described radiating applicators together with their favourable heating characteristics measured in phantom materials. Treatments are carried out in the near field of these applicators and the considerable H-fields present induce eddy-current heating in the tissues. A characteristic of near-field irradiation is that the body being treated can interact with the microwave source and affect the power radiated by it. As a result, the distance between the applicator and tissues can be critical in determining the resulting heating. This point is borne out by the findings of Kogelnik *et al.* (1978), who investigated the characteristics of local hyperthermia induced in the gluteal regions of anaesthetized pigs by commercially available 434 MHz diathermy units, and in the clinical experiences of Van Dijk *et al.* (1979).

In a controversial publication Holt (1974) claimed that microwave radiation exhibited a specific tumourcidal effect. A multiple applicator system operating at 434 MHz was the source of microwave radiation during the treatment of many patients by combined hyperthermia and ionizing radiation (Nelson and Holt, 1978). This microwave source consisted of three concentric rings of four radiating antennae and the "barrel-shaped" head could be placed around the patient at the site of interest. During microwave treatments, which were carried out before the administration of ionizing radiation, tumours were heated up to 42.5°C. Marked synergism between microwave-induced hyperthermia and ionizing radiation was claimed.

Hornback *et al.* (1977) reported results of their preliminary clinical study of combined 434 MHz and ionizing radiations. A single microwave applicator was employed, apparently similar to one described by Kebbel *et al.* (1964). Oral and skin temperatures were monitored before and after the localized hyperthermia treatments and "were found to vary considerably between patients and in the same patient on different days despite carefully controlled application of the microwave therapy". Although results were not conclusive, since only 21 patients were finally involved in the study, it was the opinion of the physicians that the effects of ionizing radiation were enhanced by hyperthermia.

Following the optimism of these clinical groups, Caldwell (1979) has suggested that the combination of 434 MHz microwaves and ionizing radiation warrants further assessment and that it may be possible to determine an optimum treatment by a rational approach.

Multiple applicators

A shortcoming of microwaves is their limited penetration in tissues with high water content. If microwave techniques are to result in effective heating at depth, it seems that it will be necessary to combine the heating patterns of several applicators placed strategically around the tissues. Such a multiple-beam microwave system is being developed by Samaras *et al.* (1978).

Anderson *et al.* (1979) have assessed theoretically the feasibility of using orthogonal, linear arrays of discrete radiating elements to produce focused microwave heating within tissue. Their calculations suggest that the temperature in a focal region with dimensions of a few centimetres could be sustained at several degrees above that of the surrounding tissue.

Experience in the use of multiple applicators has been gained through animal studies in a number of laboratories. Cheung *et al.* (1977) have shown that the use of two direct contact applicators in parallel-opposed geometry, operated at 2450 MHz in a TEM mode, can improve temperature uniformity in mouse tumours encapsulated in rectangular blocks of phantom material. Heating patterns produced in dead tissue and in the thighs of dogs by "conformal" applicators placed in opposition across these tissues have been studied by Mendecki *et al.* (1979). At 2450 MHz an approximately uniform temperature distribution (about 42°C) was achieved across 5 cm of thigh muscle. "Conformal" applicators consist of a printed circuit array of radiating elements in a volume loaded with a powder of high relative dielectric constant. A flexible bag filled with the same powder is placed in front of the array and allows the applicator to conform closely to the contours of the treated area. The heating characteristics of such applicators are determined by the distribution of the radiating elements and an applicator could be specifically designed for the treatment of a particular site.

Hand *et al.* (1979b) produced temperatures in the range 42–43°C at depths of 1–4 cm into the hind limbs of anaesthetized pigs by using two 915 MHz direct applicators in parallel-opposed geometry. Temperature variation was within 0.5°C in this region, compared with 3°C when only a single applicator was used.

SUMMARY

Capacitive coupling techniques at radiofrequencies offer the possibility of treating some deep tissue sites at the expense of localization together with the risk of heating superficial tissues excessively. If an invasive method of heating can be tolerated, localized current fields offer a relatively simple means of heating well-defined volumes of tissue. With radiofrequency induction coils, peak temperatures can occur at a depth of several centimetres and the effective penetration of this method of heating compares favourably with those of microwave techniques. The possibility of heating metallic implants to produce localized hyperthermia is attractive but a number of practical problems need to be solved.

The production and control of localized hyperthermia may be achieved effectively through microwave techniques. A compromise between penetration and localization of the heating suggests the use of a frequency in the range 400–900 MHz. Effective penetration of a few centimetres may be achieved with direct contact applicators whilst coaxial microwave devices may be used to treat sites which are accessible to catheters. The phenomenon of resonant absorption of microwaves may be used to produce differential heating in some sites. However, if deep tissue sites are to be heated effectively with microwaves, systems involving a number of microwave applicators must be developed.

APPENDIX 1

Electrical properties of tissues

The dielectric properties of a medium can be described by a complex permittivity $\epsilon=(\epsilon'-j\epsilon'')\ \epsilon_0$, where ϵ' is the dielectric constant (which influences the amount of energy that can be stored in the medium), ϵ'' is the loss factor (a measure of the energy dissipated per cycle by the medium), ϵ_0 is the permittivity of free space (8.854×10^{-12} Farad m^{-1}) and $j=\sqrt{-1}$. The conductivity of the medium σ (ohm^{-1} m^{-1}) may be expressed as $\sigma=\omega\epsilon_0\epsilon''$ ($\omega=2\pi\times$ frequency of the electromagnetic field).

Figure 4 shows the dielectric constant ϵ' and the conductivity σ of muscle tissue as functions of frequency. At frequencies lower than about 100 MHz cell membranes act as thin layers of high impedance and restrict the flow of current to the extracellular regions. Variations in ϵ' and σ in this range depend upon the cellular structure of the tissue. As the frequency increases, the capacitive reactance of the membranes decreases, resulting in an increase in the conductivity of the tissue. The decrease in ϵ' from more than 10^4 to about 10^2 may be understood by considering the period of the electromagnetic field in relation to the time required to charge the cell membranes. When the period is greater than the time constant of the charging process, the tissue exhibits a high capacitance and large value of ϵ'. When there is insufficient time for the charging process to be completed, the capacitance of the tissue and the value of ϵ' decrease.

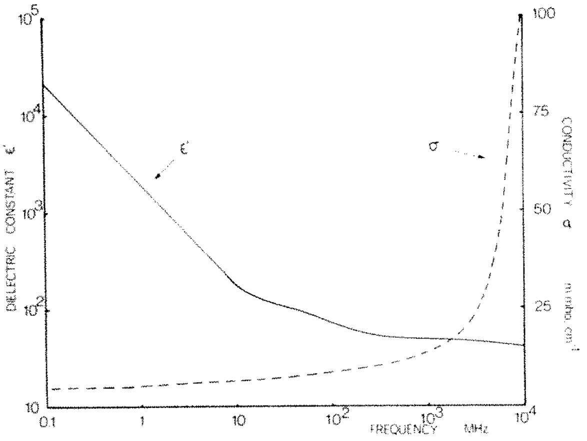


FIG. 4.

Dielectric constant ϵ' and conductivity σ (m mho cm^{-1}) of muscle tissue as functions of frequency.

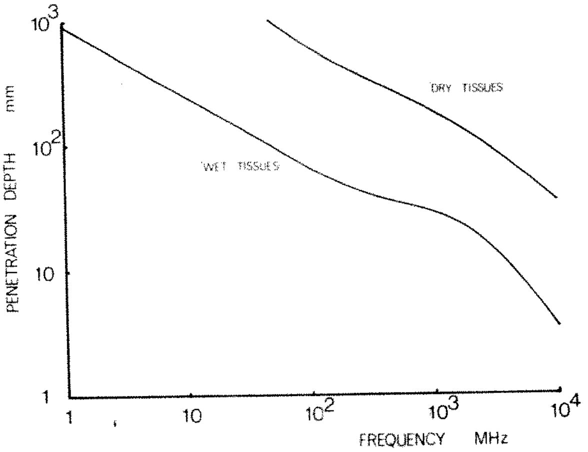


FIG. 5.

Penetration depths in tissues of high and low water content as functions of frequency. Penetration depth is the distance in which the power density is reduced by a factor $1/e^2$ (*i.e.* to approximately 0.14).

At frequencies in excess of about 100 MHz, the capacitive reactance of cell membranes is so small that they may be assumed to be short-circuited. The electrical properties of the tissue are then determined by the water, salt and protein content. Biological macromolecules have low conductivity and dielectric constant and may be considered as "dielectric holes" in the electrolyte. The slight frequency dependence of ϵ' and σ over the range 100 MHz–1 GHz may be attributed to the rotation of these large polar molecules.

The rapid increase in σ at frequencies above 1 GHz and the further decrease in ϵ' above 3 GHz arise from the polar properties of the water molecules present in the tissue.

Because of the low electrolyte content of fat, bone and other "dry" tissues, the values of ϵ' and σ for these materials are one order of magnitude lower than those for tissues of high water content. Relatively small variations in the content of both free water and water in the immediate environment of the biological macromolecules produce significant changes in ϵ' and σ for these tissues. As a result, large variations in these parameters occur from tissue to tissue.

The energy absorbed per second by unit volume of tissue (absorbed power density) is given by $\sigma E^2/2$, where E is the magnitude of the electric field within the tissue. E will vary with position, due to attenuation and possible reflections from boundaries between differing media. If the electric field is decreased from E_1 to E_2 in a thickness x of tissue, then $E_2 = E_1 \exp(-x/D)$ where D, the depth of penetration, is the distance in which the electric field is reduced by a factor of 1/e and is given by

$$D = C\sqrt{2}/\omega[(\epsilon'^2 + (\sigma/\omega\epsilon_0)^2)^{\frac{1}{2}} - \epsilon')^{\frac{1}{2}}]$$

It should be noted that the power density is reduced to approximately 14% within this distance. Figure 5 shows the variation with frequency of the penetration depth in tissues of high and low water content.

For detailed discussions of the dielectric properties of biological materials the reader is referred to the works of Schwan (1957; 1959) and Grant *et al.* (1978).

ACKNOWLEDGMENTS

I am most grateful to Drs. S. B. Field and D. K. Bewley of the Cyclotron Unit for their interest and encouragement during the preparation of this review and to Mrs. D. Wishart for excellent secretarial assistance.

REFERENCES

ANDERSON, A. P., MELEK, M., and BROWN, B. H., 1979. Feasibility of focused microwave array system for tumour irradiation. *Electronics Letters, 15*, 564–565.

ANTICH, P. P., TOKITA, N., KIM, J. H., and HAHN, E. W., 1978. Selective heating of cutaneous human tumours at 27.12 MHz. *IEEE Transactions on Microwave Theory and Techniques, MTT 26*, 569–572.

ASTRAHAN, M. A., FONG, E., GEORGE, F. W., and LIPSETT, J. A., 1978. Improving temperature uniformity of RF current field hyperthermia in homogeneous media. *Proceedings of the 3rd RTOG Hyperthermia Group Meeting*. 26–27 Nov. 1978, Chicago, Ill., USA.

BIGELOW, W. G., HOPPS, J. A., and CALLAGHAN, J. C., 1952. RF rewarming in resuscitation from severe hypothermia. *Canadian Journal of Medical Sciences, 30*, 185–193.

BIGU DEL BLANCO, J., and ROMERO-SIERRA, C., 1977. The design of a monopole radiator to investigate the effect of microwave radiation in biological systems. *Journal of Bioengineering, 1*, 181–184.

BREZOVICH, I. A., 1979. Heating of subcutaneous fat in localised current field hyperthermia with external electrodes. (*Abstract*). *Medical Physics, 6*, 352.

BRYAN, F. A., and SHINGLETON, W. W., 1963. Cancer chemotherapy heating apparatus. *Electrical Engineering, 32*, 404–407.

BURTON, C., HILL, M., and WALKER, A. E., 1971. The RF thermoseed—a thermally self-regulating implant for the production of brain lesions. *IEEE Transactions on Biomedical Engineering, BME 18*, 104–109.

CALDWELL, W. L., 1979. Evaluation of the Perth experience in treating with ionizing radiations and VHF (434 MHz) radiations. *International Journal of Radiation Oncology Biology Physics, 5*, 1919–1921.

CETAS, T. C., and CONNOR, W. G., 1978. Thermometry considerations in localized hyperthermia. *Medical Physics, 5*, 79–91.

CHEUNG, A. Y., DAO, T., and ROBINSON, J. E., 1977. Dual beam TEM applicator for direct contact heating of dielectrically encapsulated malignant mouse tumour. *Radio Science, 12, Supplement*, 6, 81–85.

CHEUNG, A. Y., and HARRISON, G. H., 1978. Bolusing materials for improved microwave hyperthermia. In *Proceedings of the 19th General Assembly of URSI: Open*

Symposium on Biological Effects of Electromagnetic Waves: 1–8 Aug. 1978, Helsinki, Finland (to be published as a supplement to *Radio Science*).

Cheung, A. Y., Robinson, J. E., McCulloch, D., and Samaras, G. M., 1978. Simultaneous far-field irradiation of multiple mouse tumours for microwave hyperthermia. In *Cancer Therapy by Hyperthermia and Radiation.* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 128–130.

Coulter, J. S., and Osborne, S. L., 1938. Wavelength in the heating of human tissues by short wave diathermy. *Journal of the American Medical Association, 110,* 639–641.

Day, P. W., Doss, J. D., Edwards, W. S., and Roth, H. B., 1976. Localised radiofrequency hyperthermia treatment of spontaneous tumors of dogs and cats. *Los Alamos Scientific Laboratory Internal Report* LA-UR-76-611.

DeLateur, B. J., Lehmann, J. F., Stonebridge, J. B., Warren, C. G., and Guy, A. W., 1970. Muscle heating in human subjects with 915 MHz microwave contact applicator. *Archives of Physical Medicine, 51,* 147–151.

Denier, A., 1936. Les ondes hertziennes ultracourtes de 80 cm. *Journal de Radiologie et d'Electrologie, 20,* 193–197.

Dickson, J. A., Calderwood, S. K., and Jasiewicz, M. L., 1977a. Radiofrequency heating of tumours in rodents. *European Journal of Cancer, 13,* 753–763.

Dickson, J. A., Shah, S. A., Waggott, D., and Whalley, W. B., 1977b. Tumor eradication in the rabbit by radiofrequency heating. *Cancer Research, 37,* 2162–2169.

Doss, J. D., and McCabe, C. W., 1976. A technique for localised heating in tissue: an adjunct to tumor therapy. *Medical Instrumentation, 10,* 16–21.

Durney, C. H., Johnson, C. C., Barber, P. W., Massoudi, H., Iskander, M. F., Lords, J. L., Ryser, D. K., Allan, S. J., and Mitchell, J. C., 1978. *Radiofrequency Radiation Dosimetry Handbook* (2nd ed.). Report SAM-TR-78-22, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

Emery, A. F., Stonebridge, J. B., Sekins, K. M., and Lehmann, J. F., 1979. Experimental and numerical studies of the elevated temperatures induced in a human leg by microwave diathermy with surface cooling. *Radio Science, 14* (6S), 297–304.

Grant, E. H., Sheppard, R. J., and South, G. P., 1978. Dielectric theory. In *Dielectric Behaviour of Biological Molecules in Solution* (Oxford University Press, London), pp. 26–56.

Guy, A. W., 1971a. Electromagnetic fields and relative heating patterns due to a rectangular aperture source in direct contact with bilayered biological tissue. *IEEE Transactions on Microwave Theory & Techniques, MTT-19,* 214–223.

1971b. Analyses of electromagnetic fields induced in biological tissues by thermographic studies on equivalent phantom models. *IEEE Transactions of Microwave Theory & Techniques, MTT-19,* 205–214.

Guy, A. W., and Lehmann, J. F., 1966. On the determination of an optimum microwave diathermy frequency for a direct contact applicator. *IEEE Transactions on Biomedical Engineering, BME 13,* 76–87.

Guy, A. W., Lehmann, J. F., and Stonebridge, J. B., 1974. Therapeutic applications of electromagnetic power. *Proceedings of the IEEE, 62,* 55–75.

Guy, A. W., Lehmann, J. F., Stonebridge, J. B., and Sorensen, C. C., 1978. Development of a 915 MHz direct contact applicator for therapeutic heating of tissues. *IEEE Transactions on Microwave Theory & Techniques, MTT-26,* 550–556.

Hand, J. W., 1977. Microwave heating patterns in simple tissue models. *Physics in Medicine and Biology, 22,* 981–987.

Hand, J. W., Robinson, J. E., Szwarnowski, S., Sheppard, R. J., and Grant, E. H., 1979a. A physiologically compatible tissue equivalent liquid bolus for microwave heating of tissues. *Physics in Medicine and Biology, 24,* 426–431.

Hand, J. W., Hopewell, J. W., Foster, J. L., and Field, S. B., 1979b. Microwave heating of musculature in the pig thigh by two 915 MHz direct contact applicators. In *Proceedings of European Group of Hyperthermia in Radiation Oncology,* Cambridge, 9–10 Sept. 1979.

Hand, J. W., Ledda, J. L., Evans, N. T. S., Cobbett, F. C. A., and Hopewell, J. W., 1980. Theoretical and experimental considerations of a radiofrequency system for heating tissues. Proc. URSI Symposium on Electromagnetic Waves and Biology. Jouy en Josas, Paris, 30 June–4 July, 1980, 249–253.

Ho, H. S., 1979. Design of aperture sources for deep heating using electromagnetic energy. *Health Physics, 37,* 743–750.

Ho, H. S., Guy, A. W., Sigelmann, R. A., and Lehmann, J. F., 1971. Microwave heating of simulated limbs by aperture sources. *IEEE Transactions on Microwave Theory & Techniques, MTT 19,* 224–231.

Holt, J. A. G., 1974. The cure of cancer—a preliminary hypothesis. *Australasian Radiology, 18,* 15–17.

Hornback, N. B., Shupe, R. E., Shidnia, H., Joe, B. T., Sayoc, E., and Marshall, C., 1977. Preliminary clinical results of combined 433 MHz microwave therapy and radiation therapy on patients with advanced cancer. *Cancer, 40,* 2854–2863.

Kantor, G., 1977. New types of microwave diathermy applicators—comparison with conventional types. In *Proceedings of the Symposium on Biological Effects and Measurement of Radiofrequency/Microwaves.* Ed. D. G. Hazzard. US Department of Health, Education and Welfare Publication (FDA) 77-8026, pp. 230–249.

Kantor, G., Witters, D. M., and Greiser, J. W., 1978. The performance of a new direct contact applicator for microwave diathermy. *IEEE Transactions on Microwave Theory & Techniques, MTT 26,* 563–568.

Kebbel, W., Krause, W., and Pätzold, J., 1964. Energieverteilung in Fett-Muskel-Schichten bei Behandlung mit längeren Dezimeterwellen im Vergleich mit den bisher in der Therapie angewendeten Hochfrequenzverfahren. *Elektromedizin, 9,* 171–179.

Kim, J. H., Hahn, E. W., Tokita, N., and Nisce, L. Z., 1977. Local tumour hyperthermia in combination with radiation therapy. 1. Malignant cutaneous lesions. *Cancer, 40,* 161–169.

Kogelnik, H. D., Prokosch, E., and Kärcher, K. H., 1978. Local hyperthermia by microwave heating (69 cm) in pigs. In *Proceedings of the 3rd RTOG Hyperthermia Group Meeting,* Chicago, November 26–27, 1978.

Krusen, F. H., Herrick, J. F., Leden, U., and Wakim, F. H., 1947. Preliminary report of experimental studies of the heating effect of microwaves (radar) in living tissues. *Proceedings of Staff Meeting at Mayo Clinic, 22,* 209–224.

Le Bourgeois, J. P. C., Convert, G., and Dufour, J., 1978. An interstitial device for microwave hyperthermia of human tumours. In *Cancer Therapy by Hyperthermia and Radiation.* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 122–124.

Lehmann, J. F., Guy, A. W., Stonebridge, J. B., and DeLateur, B. J., 1978. Evaluation of a therapeutic direct contact 915 MHz microwave applicator for effective deep tissue heating in humans. *IEEE Transactions on Microwave Theory and Techniques, MTT 26,* 556–563.

Lehmann, J. F., Guy, A. W., Warren, C. G., DeLateur, B. J., and Stonebridge, J. B., 1970. Evaluation of a microwave contact applicator. *Archives of Physical Medicine, 51,* 143–146, 151.

Lehmann, J. F., Johnston, V. C., McMillan, J. A., Silverman, D. R., Brunner, G. D., and Rathbun, L. A., 1965. Comparison of deep heating by microwaves at frequencies 2456 and 900 megacycles. *Archives of Physical Medicine, 46,* 307–314.

Lehmann, J. F., McMillan, J. A., Brunner, G. D., and Johnston, V. C., 1962. Heating patterns produced in specimens by microwaves of the frequency of 2456 MHz when applied by A, B and C directors. *Archives of Physical Medicine, 43*, 538–546.

Lehmann, J. F., Stonebridge, J. B., and Guy, A. W., 1979. A comparison of patterns of stray radiation from therapeutic microwave applicators measured near tissue-substitute models and human subjects. *Radio Science, 14* (6S), 271–283.

LeVeen, H. H., Wapnick, S., Piccone, V., Falk, G., and Ahmed, N., 1976. Tumor eradication by radiofrequency therapy. *Journal of the American Medical Association, 235*, 2198–2200.

Licht, S., 1965. *Therapeutic Heat and Cold.* Ed. S. Licht and Elizabeth Licht (New Haven, Conn.).

Lin, J. C., Guy, A. W., and Kraft, G. H., 1973. Microwave selective brain heating. *Journal of Microwave Power, 8*, 275–286.

Lin, J. C., and Kantor, G., 1978. A class of new microwave diathermy applicators. In *Proceedings of the 19th General Assembly of URSI. Symposium on Biological Effects of Electromagnetic Waves*, Helsinki, 1–8 August 1978. (p. 29 Abstract book).

Magin, R. L., 1979. A microwave system for the controlled production of local tumour hyperthermia in animals. *IEEE Transactions on Microwave Theory and Techniques, MTT 27*, 78–83.

Magin, R. L., and Kantor, G., 1977. Comparison of the heating patterns of small (2450 MHz) applicators. *Journal of Bioengineering, 1*, 493–509.

Manning, M. R., Cetas, T., Boone, M. L. M., and Miller, R. C., 1979. Clinical hyperthermia: results of the phase 1 clinical trial combining localized hyperthermia with or without radiation (high dose rate and low dose rate). Presented at ASTR 21st Annual Meeting, New Orleans, Oct. 1979. Abstract in *International Journal of Radiation Oncology Biology Physics*, 1979, *5* (suppt. 2), 173.

Marmor, J. B., Hahn, N., and Hahn, G. M., 1977. Tumor cure and cell survival after localised radiofrequency heating. *Cancer Research, 37*, 879–883.

Medal, R., Shorey, W., Gilchrist, R. K., Barker, W., and Hanselman, R., 1959. Controlled radiofrequency generator for production of localized heat in intact animal. *American Medical Association Archives of Surgery, 79*, 427–341.

Mendecki, J., Friedenthal, E., Botstein, C., Sterzer, F., Paglione, R., Nowogrodzki, M., and Beck, E., 1978. Microwave induced hyperthermia in cancer treatment: apparatus and preliminary results. *International Journal of Radiation Oncology Biology Physics, 4*, 1095–1103.

Mendecki, J., Friedenthal, E., Botstein, C., Sterzer, F., and Paglione, R., 1979. Therapeutic potential of conformal applicators for induction of hyperthermia. *Journal of Microwave Power, 14*, 139–144.

Merriman, J. H., Holmquest, H. J., and Osborne, S. L., 1934. Treatment technique in the Inductotherm. *Physiotherapy Review, 14*, 107.

Michaelson, S. M., Quinlan, W. J., Lu, S. T., Wilson, G. A., and Zagars, G., 1979. Microwave induced cranial hyperthermia and cancer therapy. *International Journal of Radiation Oncology Biology Physics, 5 (suppl. 2)*, 174 (abstract).

Moidel, R. A., Wolfson, S. K., Selker, R. G., and Weine, S. B., 1976. Materials for selective heating in a radiofrequency electromagnetic field for the combined chemothermal treatment of brain tumours. *Journal of Biomedical Materials Research, 10*, 327–334.

Nelson, A. J. M., and Holt, J. A. G., 1978. Combined microwave therapy. *The Medical Journal of Australia, 2*, 88–90.

Neymann, C. A., 1938. *Artificial Fever Produced by Physical Means: Its Development and Application.* (Charles C. Thomas, Springfield, Ill.).

Overgaard, J., 1978. Biological Effect of 27.12 MHz shortwave diathermy heating in experimental tumours. *IEEE Transactions on Microwave Theory and Techniques, MTT 26*, 523–529.

Overgaard, K., and Overgaard, J., 1972. Investigations on the possibility of a thermic tumour therapy. I. Short wave treatment of a transplanted isologous mouse mammary carcinoma. *European Journal of Cancer, 8*, 65–78.

Presman, A. S., 1970. In *Electromagnetic Fields and Life.* (Plenum Press, New York), pp. 33–44.

Robinson, J. E., Cheung, A. Y., Harrison, G. H., and Samaras, G., 1978. The response of mouse mammary tumours to microwave heating. In *Proceedings of the 19th General Assembly of URSI. Open Symposium on Biological Effects of Electromagnetic Waves.* Helsinki, 1–8 Aug. 1978 (to be published as a supplement to *Radio Science*).

Samaras, G. M., Robinson, J. E., Cheung, A. Y., Prempree, T., and Slawson, R. G., 1978. Production of controlled hyperthermal fields for cancer therapy. In *Cancer Therapy by Hyperthermia and Radiation.* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 131–133.

Schwan, H. P., 1957. Electrical properties of tissues and cells. *Advances in Biological and Medical Physics, 5*, 147–209.

1959. Alternating current spectroscopy of biological substances. *Proceedings of the IRE, 47*, 1841–1855.

Schwan, H. P., and Li, K., 1955. Variations between measured and biologically effective microwave diathermy dosage. *Archives of Physical Medicine and Rehabilitation, 36*, 363–370.

1956. The mechanism of absorption of ultrahigh frequency electromagnetic energy in tissue, as related to the problem of tolerance dose. *IRE Transactions on Medical Electronics, 4*, 45–49.

Scott, B. O., 1957. In *The Principles and Practice of Diathermy* (Heinemann, London), pp. 100–101.

Shingleton, W. W., Bryan, F. A., O'Quinn, W. L., and Krueger, L. C., 1962. Selective heating and cooling of tissue in cancer chemotherapy. *Annals of Surgery, 156*, 408–416.

Sternhagen, C. J., Doss, J. D., Day, P. W., Edwards, W. S., Doberneck, R. C., Herzon, F. S., Powell, T. D., O'Brien, G. F., and Larkin, J. M., 1978. Clinical use of radiofrequency current in oral cavity carcinomas and metastatic malignancies with continuous temperature control and monitoring. In *Cancer Therapy by Hyperthermia and Radiation.* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 331–334.

Stuchly, S. S., and Stuchly, M. A., 1978. Multimode square waveguide applicators for medical applications of microwave power. In *Proceedings of the 8th European Microwave Conference*, Paris, 4–8 Sept. 1978. (Microwave Exhibitions & Publishers Ltd., Sevenoaks, Kent), pp. 553–557.

Szmigielski, S., 1976. Use of thermography to map internal temperature distributions in rats. In *Proceedings of the International Symposium of Cancer Therapy by Hyperthermia and Radiation*, Washington, DC, April 28–30, 1975.Ed. M. J. Wizenberg, and J. E. Robinson. (American College of Radiology, Bethesda, Md.), pp. 234–235.

Szwarnowski, S., Sheppard, R. J., and Grant, E. H., 1980. A broad band microwave applicator for heating tissues. *British Journal of Radiology, 53*, 31–33.

Taylor, L. S., 1978a. Devices for microwave hyperthermia. In *Cancer Therapy by Hyperthermia and Radiation.* Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 115–117.

1978b. Electromagnetic syringe. *IEEE Transactions on Biomedical Engineering, BME 25*, 303–304.

Thom, H., 1966. *Introduction to Shortwave and Microwave Therapy.* (Charles C. Thomas, Springfield, Ill.).

Tinga, W. R., and Nelson, S. O., 1973. Dielectric properties of materials for microwave processing—tabulated. *Journal of Microwave Power*, *8*, 23–65.

VAN DIJK, C., VAN RHOON, G., BONKE-SPIT, L., and REINHOLD, H. S., 1979. Some problems encountered with the application of hyperthermia in patients. In *Proceedings of the European Group of Hyperthermia in Radiation Oncology*, Cambridge, 9–10 Sept. 1979.

VAN KOUGHNETT, A. L., and WYSLOUZIL, W., 1972. A waveguide TEM mode exposure chamber. *Journal of Microwave Power*, *7*, 381–383.

VON ARDENNE, M., 1978. On a new physical principle for selective local hyperthermia of tumor tissues. In *Cancer Therapy by Hyperthermia and Radiation*. Ed. C. Streffer (Urban and Schwarzenberg, Munich), pp. 96–104.

III. Ultrasound

By Gail ter Haar, Ph.D. and J. W. Hand, Ph.D.

The ability of ultrasound to heat tissues has been known and utilized for many years (Freundlich *et al.*, 1932; Pohlman *et al.*, 1939; Bergmann 1954).* Ultrasound in the frequency range 0.5–5 MHz has widespread uses as a therapeutic agent in physical medicine (Summer and Patrick, 1964; Lehmann *et al.*, 1978; Wells, 1977). Until recently, it was thought that the benefits derived from therapeutic ultrasound were due only to thermal effects. However, there is now good evidence that some changes may be due to non-thermal mechanisms (ter Haar *et al.*, 1980; Kremkau, 1979). Focused ultrasound may be used for producing lesions at depth in soft tissues such as the brain (Fry, 1978) without damage to the intervening tissue.

In an excellent historical survey of the role of ultrasound in cancer therapy, Kremkau (1979) traces its usage from the first report by Szent-Györgi (1933) through to its status in 1979. He also reviews some of the published clinical data.

The first report of changes in biological organisms produced by ultrasound was published in 1927 when Wood and Loomis described changes in *Spirogyra*, fish and frogs due to 300 kHz ultrasound. This work was stimulated by the unpublished work of Langevin. In 1928 Harvey and Loomis published observations of damage in small biological organisms after exposure to 406 kHz ultrasound. Some of the effects seen were thought to be due to heating.

PHYSICS OF ULTRASOUND

Ultrasound is a form of mechanical energy that propagates through tissue as a pressure wave. It is generated by the application of a high-frequency voltage across a piezo-electric transducer. The transducer face, acting like the end of a piston, vibrates in response to the high-frequency signal and creates a pressure wave. Frequencies in the range 0.5–10 MHz are most commonly used for medical purposes. Sound travels through water and soft tissues as longitudinal waves. In bone, however, both transverse (shear) and longitudinal waves are possible. There may be conversion from longitudinal to shear wave propagation when a wave passes from soft tissue to bone.

The velocity at which an ultrasonic wave propagates through soft tissues is about 1500 m s^{-1} (the mean value at 37°C is ~1570 m s^{-1} in non-fatty soft tissues and ~1430 m s^{-1} in fat). This leads to wavelengths of 3 mm at 0.5 MHz and 0.15 mm at 10 MHz. André *et al.* (1980) give a value for the human femur of about 3.3×10^3 m s^{-1}. This leads to wavelengths of 1.6 mm at 0.5 MHz and 0.33 mm at 10 MHz.

As an ultrasonic beam travels through tissue, the total energy in the beam is attenuated. In a homogeneous medium the energy of a perfectly collimated beam would decrease exponentially with the distance travelled in the tissue (see Appendix 2). The intensity at a position x in the tissue is given by

$$I=I_0e^{-\mu x} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where I_0 is the intensity at point $x=0$ and μ is the intensity attenuation coefficient. The two main sources of energy loss are absorption and scattering. It is the absorption that leads to the direct generation of heat. Some of the energy scattered out of the primary beam will be absorbed elsewhere in the tissue.

Values of attenuation coefficients for normal tissues can be found in the literature. Two recent compilations are by Goss *et al.* (1978; 1980). Very few data are available for human tissues or for tumours. Typical values of attenuation coefficients are shown in Table AI (Appendix 2). The data available for absorption coefficients are extremely sparse. Estimates of the contribution that absorption makes to total attenuation vary from 30% (Goss *et al.*, 1979) to 70% (Hill *et al.*, 1978).

The interaction of ultrasound with tissue can broadly be divided into two classes of mechanism: those due to heating and those due to non-thermal effects. Estimates of the magnitude of the increases in temperature induced by ultrasound are given in Appendix 2.

---

*References to the literature will be found following Part III on p. 465.

The main non-thermal mechanisms thought to occur in tissue are due to cavitation (Neppiras, 1980; Coakley and Nyborg, 1978), acoustic streaming and radiation force (Dunn and Pond, 1978). There is evidence that these effects may be of additional benefit in cancer therapy (Kremkau, 1979; ter Haar *et al.*, 1980). Only thermal effects are discussed in this paper.

The intensity of an ultrasonic beam is defined as the energy fluence and is usually specified in watts cm^{-2}. In conventional ultrasonic physiotherapy, spatial average intensities up to 3 W cm^{-2} are used. For pulse-echo diagnostic ultrasound, intensities averaged over space and time are typically about 20 mW cm^{-2}.

The space-averaged intensity in an ultrasonic therapy beam may be measured using a radiation balance (Hill, 1970; Shotton, 1980). Beam profiles are measured using small pressure sensitive hydrophones, or small heat sensitive devices.

Since ultrasound is rapidly attenuated in air at the frequencies used clinically, a coupling medium is required between the ultrasonic transducer and the tissue to be treated. This may be an aqueous gel (for contact applications) or a container of degassed water. It is essential that no air pockets exist between the irradiating head and the tissue.

ULTRASONIC TRANSDUCERS

Ultrasonic transducers for medical therapy are usually cut from a piezo-electric material such as lead zirconate titanate 4 (PZT4). The device is driven to vibrate in its thickness mode. (Radial modes of vibration are also possible, but these generally occur at lower frequencies.) For maximum energy output, the transducer element is half a wavelength thick and backed by air. The efficiency of transduction of PZT4 (that is, the ratio of acoustical power obtained from the crystal to the electrical power applied) is typically greater than 50%.

Plane transducers

The most commonly used transducers are in the form of circular discs with plane faces. The fields from such transducers can be calculated assuming that the plane faces respond linearly to an applied sinusoidal voltage and vibrate as a whole with uniform amplitude and phase. The resultant field is commonly described in terms of two regions: the near field (Fresnel zone) and the far field (Fraunhofer zone).

In the near field, interference effects close to the transducer face result in very complex axial and transverse profiles. In the far field, the intensity varies smoothly, with the intensity on axis dropping off as the inverse square of distance in a non-attenuating medium. The directivity function in the far field, D_s, is given by

$$D_s = \frac{2 J_1 (2\pi a \sin \theta/\lambda)}{2\pi a \sin \theta/\lambda} \quad . \quad . \quad . \quad . \quad (2)$$

where J_1 is the first order Bessel function, a is the radius of the transducer, θ is the angle that the line joining the measuring point with the centre of the transducer face makes with the axis and λ is the wavelength of sound in the medium concerned.

The transition between the near and far fields is usually taken to be at the last axial maximum which occurs approximately at a distance a^2/λ from the transducer. Transducers most commonly used for therapy have diameters of 3–6 cm. At 1 MHz the near field in soft tissue extends 15 cm for a 3 cm diameter transducer, and 60 cm for a 6 cm diameter transducer. At 5 MHz the near field of a 3 cm transducer extends to 75 cm.

In practice, field patterns from plane circular transducers differ from those calculated theoretically. Reasons for this include factors such as the crystal mounting and soldered electrode connections. It is essential, therefore, that each transducer field should be characterized by measurement, as local hot spots may arise. Figure 6 shows measured field plots for three plane transducers at different frequencies. It can be seen that the beam narrows with increasing frequency, and that the complex near-field region extends furthest at higher frequencies. It should be noted that the temperature distribution resulting from a non-uniform ultrasonic field is modified by thermal conduction and blood flow. Marmor *et al.* (1979) were unable to detect variations in temperature in a tumour subjected to 20% variations in intensity.

The depth of tissue that a beam will traverse before its energy is reduced to e^{-2} of its initial value is known as the penetration depth. Representative values are shown in Table III. It should be borne in mind that considerable variations will occur with the composition and structure of the particular tissue.

The majority of the work on ultrasonic hyperthermia that has been published to date has made use of plane transducers (see, for example, Dittmar, 1949; Smachlo *et al.*, 1979; Woeber, 1965).

In a preclinical study involving cats and dogs (Marmor *et al.*, 1978), spontaneous tumours less than 2 cm deep and less than 2 cm in diameter were treated with 0.7–5.0 MHz ultrasound. The transducers were 2 cm diameter discs held in a metal housing. Water circulated through an acrylic cylinder attached to the front of the transducer. A thin flexible membrane provided the acoustic window. Uniform temperature distributions were achieved across the diameter of the tumour at a constant depth, despite a 30% variation of free field intensity across the transducer face.

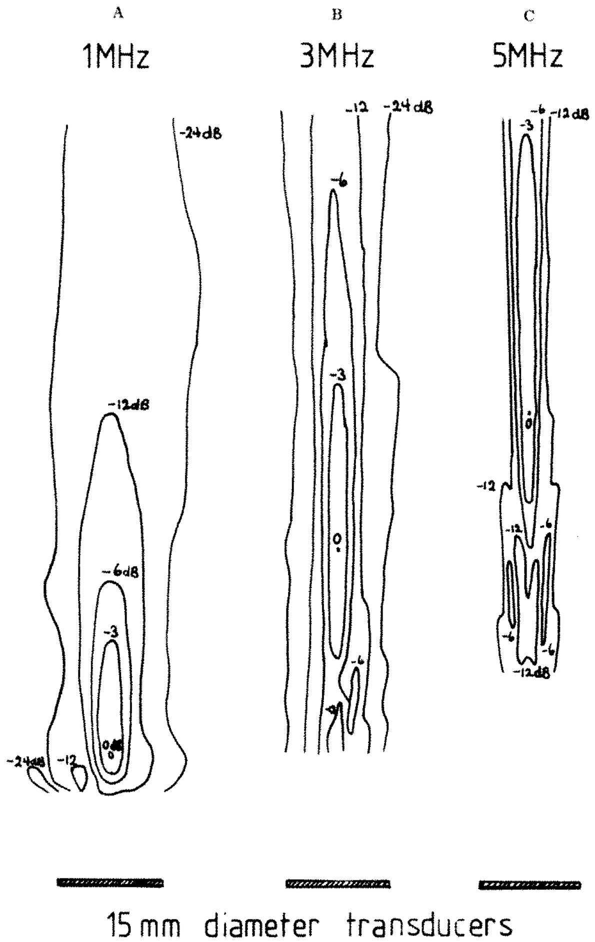


FIG. 6.

Field plots for three plane transducers (15 mm diameter) driven at (A) 1 MHz, (B) 3 MHz, (C) 5 MHz. Contours are shown for intensity levels 3 dB, 6 dB, 12 dB and 24 dB below the peak intensity. A level of −3 dB corresponds to a reduction in intensity to 50%, −6 dB to 25% etc.

TABLE III

PENETRATION DEPTH

Tissue type	Frequency		
	1 MHz	3 MHz	5 MHz
Fat	14 cm	5.5 cm	3.7 cm
Muscle	12.5–4.5 cm	3–2.2 cm	1.69–1.4 cm
Bone	0.69–0.46 cm	—	—

Using this system "hot spots" were obtained around bone or air. The same workers (Marmor *et al.*, 1979) have used a similar system to heat patients. The transducers in this case were up to 4 cm in diameter. Temperature differences of 1–2°C between the centre and periphery of 4 cm tumours were seen, for central temperatures of 43–45°C. Some patients experienced pain when the irradiated tumours overlay bone or nerve. This is to be expected because of selective heating in these tissues and at their interfaces (Lehmann *et al.*, 1966; Rosenberger, 1950) and may be overcome by using a more localized heating beam.

Although the use of plane transducers does not allow selective heating at depth, the low absorption of ultrasound in superficial tissues means that reasonable penetration may be achieved without undue surface heating. Where more localized deep heating is required, focused ultrasound may be used.

Focused transducers

One advantage of ultrasound lies in its ability to heat well-defined volumes of tissue using focusing techniques. Focusing may be achieved by using a (concave) bowl transducer, a plane transducer and a lens, or a plane transducer and a mirror. Alternative methods of selective heating of localized volumes include multi-element arrays or multiple beam techniques.

1. *Focused-bowl transducers.* The simplest method of achieving a focused ultrasonic field is by use of a spherical curved shell of piezo-electric material. Calculation of the field distribution from such transducers has been described by O'Neil (1949), Penttinen and Luukkala (1976) and Kossoff (1979). The focus of these transducers lies on the central axis, near the centre of curvature of the bowl (Fig. 7). As $2\pi h/\lambda$ increases (where h is the depth of the shell), the focal point approaches the centre of curvature C. A good estimate of the intensity at the focus is given by the intensity at C, I_c, which is given by

$$I_c/I_0=(2\pi h/\lambda)^2 \quad . \quad . \quad . \quad . \quad (3)$$

I_0 is the average intensity at the transducer surface. I_c/I_0 is known as the gain factor, G.

The width of the focal region, W, is given by

$$W=1.22\,R\lambda/a \quad . \quad . \quad . \quad . \quad (4)$$

where R is the radius of curvature and a is the radius

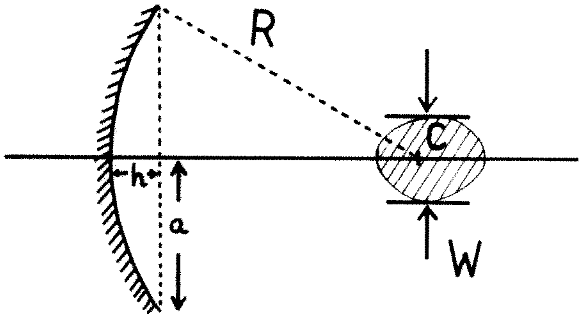


FIG. 7.

Diagram illustrating the geometry of a focused bowl transducer. *C*—centre of curvature; *h*—depth of shell; *a*—radius of the transducer; *R*—radius of curvature of bowl; *W*—width of focal region.

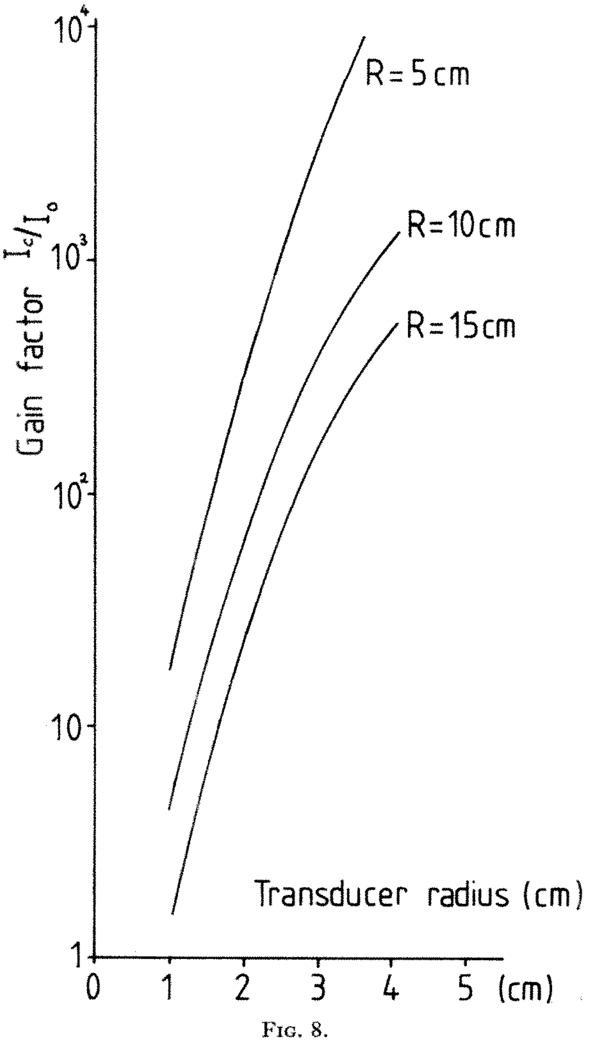


FIG. 8.

Variation of gain factor (*G*) with transducer radius (*a*) for different radii of curvature (*R*) at 1 MHz.

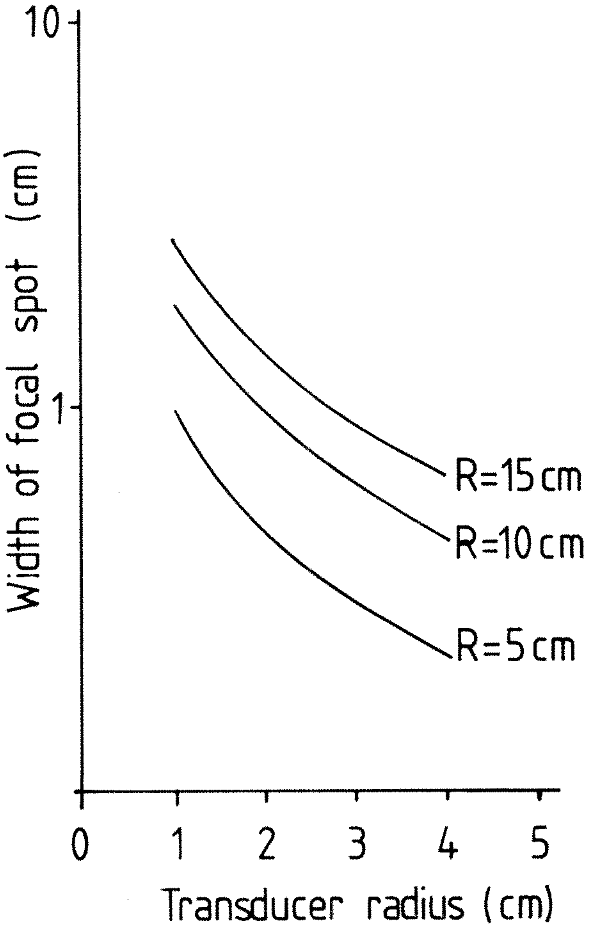


FIG. 9.

Variation of focal spot width (*W*) with transducer radius (*a*) for different radii of curvature (*R*) at 1 MHz.

of the transducer. This expression holds if $a \gg \lambda$. Thus, for example, for a 1 MHz ultrasonic beam, and a bowl with $R = 10$ cm, $a = 2.5$ cm, $h = 3.0$ mm, $G = 158$, and $W = 0.73$ cm, whereas for $R = 10$ cm, $a = 5$ cm, $h = 1.34$ cm, $G = 3.15 \times 10^3$ and $W = 0.37$ cm. Kossoff *et al.* (1965) have shown that 84% of the total energy lies in the main lobe of diameter W at the focal point.

The way in which I_c/I_0 and W vary with a, R and f are shown graphically in Figs. 8, 9 and 10. A beam profile for a 2 cm radius spherical bowl of focal length 15 cm is shown in Fig. 11.

In general, the focal volumes produced from bowl transducers are smaller than the tumour volumes to be treated. Lele (1975) has overcome this problem by scanning a focused transducer mechanically, under computer control, over the target volume. The computer optimizes the frequency, power level, trajectory

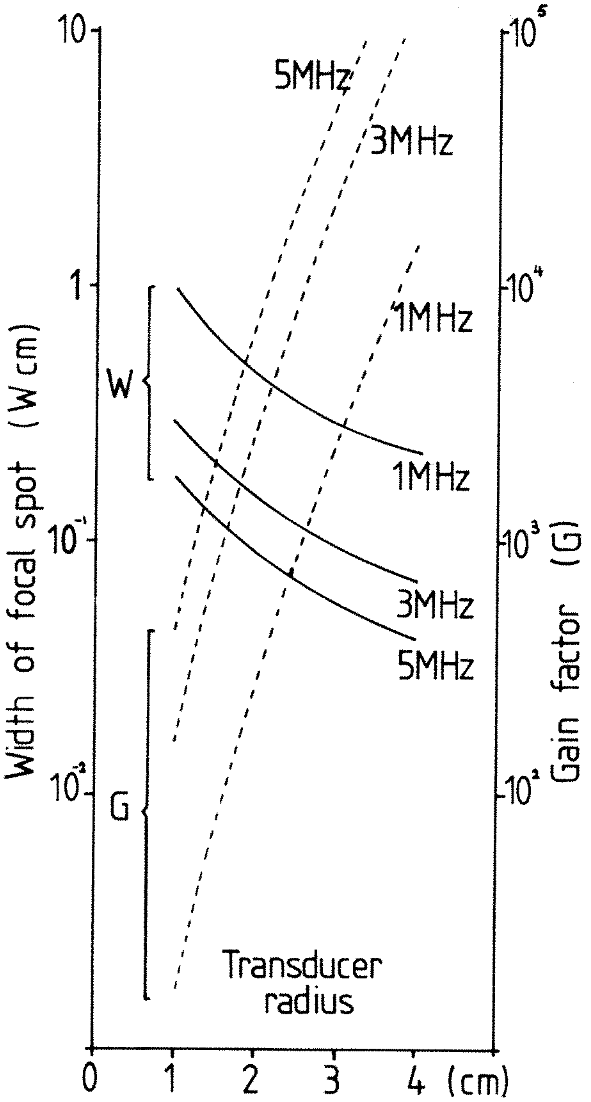


FIG. 10.

Graphs showing the frequency dependence of the variation of gain factor (G) and focal spot width (W) with transducer radius (a) ($R=5$ cm).

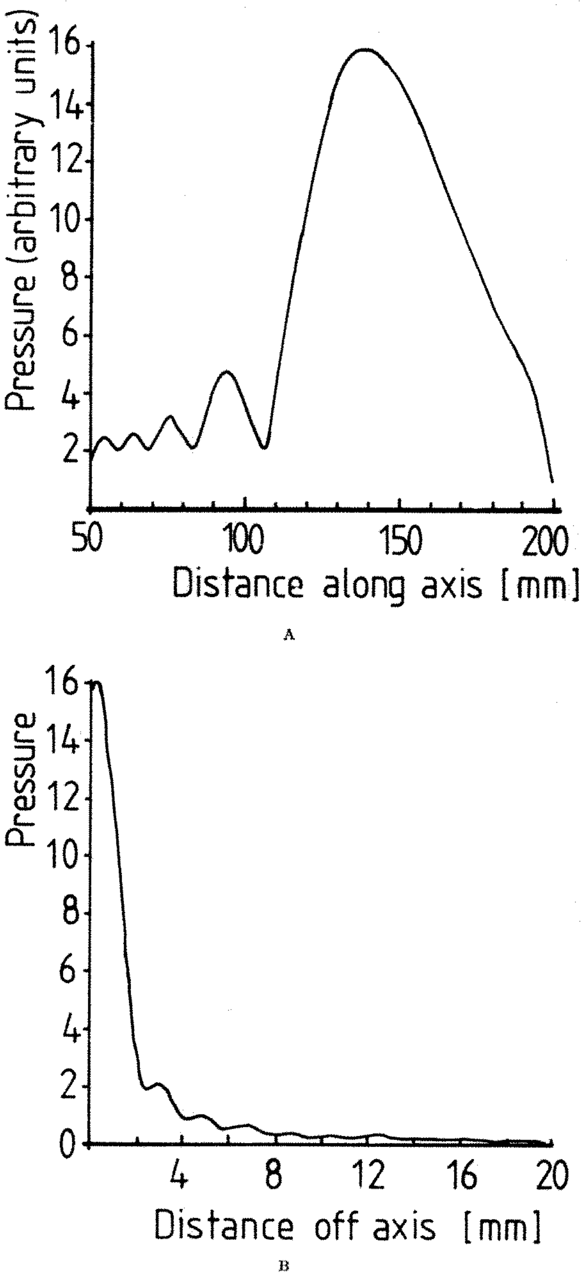


FIG. 11.

Theoretical field distributions from a 2 cm radius spherical bowl with focal length 15 cm. (A) Axial distribution. (B) Transverse profile at the focus.

and speed of the transducer. This system can produce temperature distributions of the desired level (± 0.1°C) in tissue volumes up to 10 cm in diameter (Lele, 1980).

Although focused-bowl transducers can give well localized heated volumes (Robinson and Lele, 1972), they do not provide any flexibility of focal depth.

2. *Lens systems.* Ultrasonic lenses are usually made from solids in which the velocity of sound is greater than in water. Concave lenses are therefore used in order to obtain a converging beam. The easiest lenses to construct are plano-cancave. The focal length, F, of such lenses is given by the expression

$$F=R/(1-n) \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where R is the radius of curvature of the concave face, and n is the refractive index, given by the ratio of the sound velocity in the lens material to that in the surrounding medium. A discussion of such lens systems may be found in reviews by Fry and Dunn (1962) and Kikuchi (1978).

The main limitation of acoustic lens systems is absorption of sound in the lens material. Lenses are usually made of polystyrene (Lucite) or Perspex. Where small apertures are needed, the concave face may be spherical. For larger apertures, where spherical aberration is important, the face should be ellipsoidal. Wells (1977) shows that, for a polystyrene lens with focal length 10 cm, $R=3.6$ cm, at 1 MHz, $a=3.36$ cm, the length of the focal spot is 2.72 cm and the width is 0.22 cm. The intensity at the focus is about 750 times that at the threshold. At 3 MHz, $a=2.5$ cm, the focal spot length is 1.3 cm, the width is 0.1 cm and the intensity gain is 2000.

Where plane transducers are used with plano-concave lenses, maximum power transmission is obtained when the transducer and the lens are separated by a quarter of a wavelength of a material chosen to provide an acoustic impedance match.

Details of a transducer/lens combination used to produce sharply defined zones of necrosis in rat liver and rabbit liver and kidney have been given by Linke *et al.* (1973). Lehmann and Krusen (1955) have described a similar system to treat Ehrlich's ascitic carcinoma in the mouse.

3. *Mirrors.* Although ultrasonic beams may be focused using mirror systems (Wells, 1977; Kikuchi, 1978), these methods are not suitable in general for hyperthermia.

4. *Crossed beam techniques.* Localized heating may be achieved using several plane transducers arranged in such a way that the beams cross at the volume to be heated. This system may be cumbersome, but does allow some flexibility in depth and volume of heating.

5. *Phased arrays.* Phased-array technology is now well developed for diagnostic ultrasound (Wells, 1977). The expertise gained from these transducers may be used to obtain a versatile ultrasonic heating system. The array may consist of different transducer elements, or of elements etched on a common substrate.

The beam from a linear array of transducer elements may be swept electronically across a plane if a variable phase difference is applied between the elements. If a two-dimensional array is used, suitable choice of phasing of the elements allows focusing of the beam in the required plane.

If the transducer consists of concentric ring sources (an annular array), focusing of the beam at any point along the axis may be achieved by suitable phasing of the active periods of the individual elements.

SUMMARY

The use of ultrasonic hyperthermia in the clinic is so far largely unexplored. Ultrasound transducer technology provides a number of versatile ways in which required volumes in soft tissue may be heated. The main limitation with ultrasound heating lies in its inability to traverse bone or air. If large volumes of tissue are to be heated either mechanical or electronic beam steering is necessary.

ACKNOWLEDGMENTS

We should like to thank Dr. C. R. Hill for his help and encouragement during preparation of this review, and Dr. J. C. Bamber for providing the data shown in Fig. 6.

APPENDIX 2

The energy in an ultrasonic beam is attenuated by passage through tissue. For plane waves travelling through homogeneous tissue, the intensity at any position x is given by

$$I(x)=I_0e^{-\mu x} \quad . \quad . \quad . \quad . \quad . \quad (A1)$$

where I_0 is the intensity at the point $x=0$, and μ is the intensity attenuation coefficient. (Attenuation is also sometimes described in terms of amplitude attenuation coefficient, α, where $\mu=2\alpha$.)

Energy loss in the medium is due both to absorption and to scattering of sound out of the main beam, and the attenuation coefficient may be written

$$\mu=\mu_a+\mu_s \quad . \quad . \quad . \quad . \quad . \quad (A2)$$

where μ_a is the absorption coefficient and μ_s is the scattering coefficient and μ may be expressed in units of cm^{-1} or decibels/cm ($dB\ cm^{-1}$) where $1.0\ cm^{-1}=4.3\ dB\ cm^{-1}$.

Typical values of intensity attentuation coefficient for human tissues are shown in Table AI. In general μ varies approximately linearly with increasing frequency for fat and soft tissues in the range 500 kHz–10 MHz. For bone, the frequency dependence is more complex (Wells, 1977), varying in an approximately quadratic fashion up to 2 MHz and thereafter more nearly linearly.

The acoustic properties of lung tissue differ from those of other soft tissues. According to Dunn (1974) the attenuation in lung tissue is high and dependent upon degree of inflation. For deflated canine lung tissue $\mu=4\ cm^{-1}$ at 1 MHz increasing exponentially to $12\ cm^{-1}$ at 5 MHz.

TABLE AI

TYPICAL INTENSITY ATTENUATION COEFFICIENTS

Tissue type	Frequency		
	1 MHz	3 MHz	5 MHz
Fat	0.14–0.18 cm^{-1}	0.36 cm^{-1}	0.54 cm^{-1}
Muscle	0.16–0.44 cm^{-1}	0.60–0.90 cm^{-1}	1.18–1.40 cm^{-1}
Bone	2.88–4.30 cm^{-1}	—	—

Values for human tissue as listed by Goss *et al.* (1978;1980)

The reflection of ultrasound at an interface between media is determined by the characteristic acoustic impedances (density × velocity of sound) of the media. The velocities of sound in soft tissues (excluding lung) are close to that in water (1500 m s^{-1}) and the variations in velocity arise from the protein and lipid content of different tissues. The velocity of sound in fatty tissues is approximately 10% lower than that in other soft tissues.

The properties of bone and lung differ considerably from those of most soft tissues. The longitudinal speed of sound in bone is approximately twice that in soft tissue, whilst in lung tissue it is 40–80% of the velocity in other soft tissues and is dependent upon acoustic frequency and degree of pulmonary inflation.

For detailed discussions of the acoustic properties of biological materials the reader is referred to the works of Dunn and O'Brien (1978) and Wells (1977).

It can be shown, for tissue in which no heat is lost by thermal conduction or blood flow, that the rate of temperature rise is given by the equation

$$\frac{\mathrm{d}T}{\mathrm{d}t} = \frac{\mu I}{\rho C} \quad . \; . \; . \; . \; . \; . \quad \text{(A3)}$$

where I is the intensity, ρ is the tissue density and C the heat capacity. For the purposes of this calculation, attenuation is taken to be largely due to absorption.

If soft tissue with $\mu \sim 0.2$ cm^{-1} is irradiated with an ultrasonic beam of intensity 1 W cm^{-2}, the rate of temperature rise is 0.048°C s^{-1} (2.87°C min^{-1}) ($\rho = 1$ g cm^{-3}, $C = 4.18$ J g^{-1} per °C).

The effect of variation of acoustic intensity, frequency, attenuation coefficient and blood flow have been discussed from a theoretical viewpoint elsewhere (ter Haar, 1979; Schwan *et al.*, 1953).

REFERENCES

ANDRÉ, M. P., CRAVEN, J. D., GREENFIELD, M. A., and STERN, R., 1980. Measurement of the velocity of ultrasound in the human femur *in vivo*. *Medical Physics*, *7*, 324–330.

BERGMANN, L., 1954. *Der Ultraschall* (Hirzel Verlag, Stuttgart).

COAKLEY, W. T., and NYBORG, W. L., 1978. Cavitation: dynamics of gas bubbles; applications. In *Ultrasound: Its Applications in Medicine and Biology*, I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 77–159.

DITTMAR, C., 1949. Über die Wirkung von Ultraschallwellen auf tierische Tumoren. *Strahlentherapie*, *78*, 217–230.

DUNN, F., 1974. Attenuation and speed of ultrasound in lung. *Journal of the Acoustical Society of America*, *56*, 1638–1639.

DUNN, F., and O'BRIEN, W. D., 1978. Ultrasonic absorption and dispersion. In *Ultrasound: Its Applications in Medicine and Biology*, I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 393–439.

DUNN, F., and POND, J. B., 1978. Selected non-thermal mechanisms of interaction of ultrasound in biological media. In *Ultrasound: Its Applications in Medicine and Biology*, I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 539–559.

FREUNDLICH, H., SOLLNER, K., and ROGOWSKI, F., 1932. Einige biologische Wirkungen von Ultraschallwellen. *Klinische Wochenschrift*, *11*, 1512–1513.

FRY, F. J., 1978. Intense focused ultrasound: its production, effects and utilization. In *Ultrasound: Its Applications in Medicine and Biology*, I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 689–741.

FRY, F. J., and DUNN, F., 1962. Ultrasound—analysis and experimental methods in biological research. In *Physical Techniques in Biological Research*. Ed. L. Nastuk (Academic Press, New York), pp. 307–410

GOSS, S., JOHNSTON, R., and DUNN, F., 1978. Comprehensive compilation of empirical ultrasonic properties of mammalian tissues. *Journal of the Acoustical Society of America*, *64*, 423–457.

GOSS, S. A., FRIZZELL, L. A., and DUNN, F., 1979. Ultrasonic absorption and attenuation in mammalian tissues. *Ultrasound in Medicine and Biology*, *5*, 181–186.

GOSS, S. A., JOHNSTON, R. L., and DUNN, F., 1980. Compilation of empirical ultrasonic properties of mammalian tissues. II. *Journal of the Acoustical Society of America*, *68*, 93–108.

TER HAAR, G. R., 1979. Temperature distributions obtainable in tissue as a result of ultrasonic irradiation. *Proceedings of the Meeting of the European Group of Hyperthermia in Radiation Oncology*, Cambridge, September 1979 (to be published).

TER HAAR, G. R., STRATFORD, I. J., and HILL, C. R., 1980. Ultrasonic irradiation of mammalian cells *in vitro* at hyperthermic temperatures. *British Journal of Radiology*, *53*, 784–789.

HARVEY, E. N., and LOOMIS, A. L., 1928. High frequency sound waves of small intensity and their biological effects. *Nature* (London), *12*, 622–624.

HILL, C. R., 1970. Calibration of ultrasonic beams for biomedical applications. *Physics in Medicine and Biology*, *15*, 241–248.

HILL, C. R., CHIVERS, R. C., HUGGINS, R. W., and NICHOLAS, D., 1978. Scattering of ultrasound by human tissue. In *Ultrasound: Its Applications in Medicine and Biology*, I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 441–493.

KIKUCHI, Y., 1978. Transducers for ultrasonic systems. In *Ultrasound: Its Applications in Medicine and Biology*. I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 289–342,.

KOSSOFF, G., 1979. Analysis of focusing action of spherically curved transducers. *Ultrasound in Medicine and Biology*, *5*, 359–365.

KOSSOFF, G., ROBINSON, D. E., and GARRETT, W. J., 1965. Ultrasonic two dimensional visualisation technique. *IEEE Transactions Sonics–Ultrasonics*, *SU-12*, 31–37.

KREMKAU, F. W., 1979. Cancer therapy with ultrasound: a historical review. *Journal of Clinical Ultrasound*, *7*, 287–300.

LEHMANN, J. F., DE LATEUR, B. J., and SILVERMAN, D. R., 1966. Selective heating effects of ultrasound in human beings. *Archives of Physical Medicine and Rehabilitation*, *47*, 331–339.

LEHMANN, J. F., and KRUSEN, F. H., 1955. Biophysical effects of ultrasonic energy on carcinoma and their possible significance. *Archives of Physical Medicine and Rehabilitation*, *36*, 452–459.

LEHMANN, J. F., WARREN, C. G., and GUY, A. W., 1978. Therapy with continuous wave ultrasound. In *Ultrasound: Its Applications in Medicine and Biology*. I. Ed. F. J. Fry (Elsevier, Amsterdam), pp. 561–587.

LELE, P. P., 1975. Hyperthermia by ultrasound. In *Proceedings of the International Symposium on Cancer Therapy by Hyperthermia and Radiation*, Washington, D.C., April 28–30, 1975. Ed. M. J. Wizenberg and J. E. Robinson (American College of Radiology, Bethesda, Md.), 168–178.

1980. Induction of deep, local hyperthermia by ultrasound and electromagnetic fields—problems and choices. *Radiation and Environmental Biophysics*, *17*, 205–217.

LINKE, C. A., CARSTENSEN, E. L., FRIZZELL, L. A., ELBADAWI, A., and FRIDD, C. W., 1973. Localised tissue destruction by high intensity focused ultrasound. *Archives of Surgery*, *107*, 887–891.

MARMOR, J. B., POUNDS, D., HAHN, N., and HAHN, G. M., 1978. Treating spontaneous tumours in dogs and cats by ultrasound induced hyperthermia. *International Journal of Radiation Oncology Biology Physics*, *4*, 967–973.

MARMOR, J. B., POUNDS, D., POSTIC, T. B., and HAHN, G. M., 1979. Treatment of superficial human neoplasms by local hyperthermia induced by ultrasound. *Cancer*, *43*, 188–197.

NEPPIRAS, E. A., 1980. Acoustic cavitation. *Physics Reports*, *61*, No. 3, 159–251.

O'NEIL, H. T., 1949. Theory of focussing radiators. *Journal of the Acoustical Society of America*, *21*, 516–526.

PENTTINEN, A., and LUUKKALA, M., 1976. Sound pressure near the focal area of an ultrasonic lens. *Journal of Physics D: Applied Physics*, *9*, 1927–1936.

POHLMAN, R., RICHTER, R., and PAROW, E., 1939. Über die Ausbreitung und Absorption des Ultraschalls in menschlichen Gewebe und seine therapeutische Wirkung in Ischias und Plexus-neuralgia. *Deutsche Medizinische Wochenschrift*, *65*, 251–254.

ROBINSON, T. C., and LELE, P. P., 1972. An analysis of lesion development in the brain and in plastics by high-intensity focused ultrasound at low megahertz frequencies. *Journal of Acoustical Society of America*, *51*, 1333–1351.

ROSENBERGER, H., 1950. Über den Wirkungsmechanismus der Ultraschallbehandlung, insbesondere bei Ischias und Neuralgien. *Der Chirurgie*, *21*, 404–406.

SCHWAN, H. P., CARSTENSEN, E. L., and LI, K., 1953. Heating of fat-muscle layers by electromagnetic and ultrasonic diathermy. *Communications and Electronics*, *8*, 483–487.

SHOTTON, K. C., 1980. A tethered float radiometer for measuring the output power from ultrasonic therapy equipment. *Ultrasound in Medicine and Biology*, *6*, 131–133.

SMACHLO, K., FRIDD, C. W., CHILDS, Z., HARE, J. D., LINKE, C. A., and CARSTENSEN, E. L., 1979. Ultrasonic treatment of tumors. I. Absence of metastases following treatment of a hamster fibrosarcoma. *Ultrasound in Medicine and Biology*, *5*, 45–49.

SUMMER, W., and PATRICK, M. K., 1964. *Ultrasonic Therapy* (Elsevier, Amsterdam).

SZENT-GYÖRGI, A., 1933. Chemical and biological effects of ultrasonic radiation. *Nature*, *131*, 278.

WELLS, P. N. T., 1977. *Biomedical Ultrasonics* (Academic Press, London).

WOEBER, K., 1965. The effect of ultrasound in the treatment of Cancer. In *Ultrasonic Energy*. Ed. E. Kelly (University of Illinois Press, Urbana, Ill.), pp. 135–149.

WOOD, R. W., and LOOMIS, A. L., 1927. The physical and biological effects of high-frequency sound waves of great intensity, *4*, 417–436.

Book review

Oncology Supplement, Scientific Foundations of Oncology. Eds. Sir Thomas Symmington and R. L. Carter, pp. x+173, 143 figs., 31 tables, 1980 (Heinemann, London) £16·00. ISBN 0-433-05149-3

An increasingly important duty of experienced scientists and research workers is making effective reviews of certain areas within their own speciality in a form which is intelligible to research workers in other disciplines. The field of oncology spans a large number of disciplines and this book has provided us with reviews in eleven areas of topical interest ranging from basic work in molecular oncology to some aspects of epidemiology. It is a very readable, well-illustrated collection of papers, containing much material of interest to research workers both inside and outside the general field of oncology. The close interaction in the present-day approach to the molecular biology of cancer is exemplified by the first, well illustrated chapter by Harris Bush. Another topical subject of considerable commercial and environmental interest is a review of short-term tests in the prediction of carcinogenicity by B. J. Dean. An updated review of the association between bovine neoplasia and bracken is written by Grimshaw and Evans, including the interesting distribution in Western Scotland described by Pirie in 1973. Although a potential link with human cancer may be implied here, a most useful survey of endogenous carcinogens mostly proven in human cancer is reviewed separately by M. J. Hill. It is remarkable how many apparently diverse etiological origins can be focused on to N-nitroso compounds as a potentially guilty species.

Transplantation of human tumours into immunosuppressed or immunologically privileged sites would appear to offer the experimentalist a most valuable system in xenografting. To test chemotherapeutic agents in such a system would appear to be attractive, but in their present state the task is somewhat expensive and formidable. The many aspects of this complex subject are well reviewed by B. C. Giovanella. A detailed study of pre-malignancy in heart disease is surveyed by S. A. Halter and D. L. Page, while the patterns and mechanisms of bone destruction during skeletal metastases are discussed by C. C. Easty and R. L. Carter.

The field of hypoxic-cell sensitizers has stimulated the interest of many chemists, primarily due to the close link of radiation sensitivity to reduction-oxidation reactions already well understood by this group of scientists. I. J. Stratford describes many of the interesting experimental aspects. The somewhat futuristic and exciting field of computed tomography has clearly attracted many devotees where the money has become available. The remarkable X-ray pictures derived from this machine are discussed and well illustrated in a good review by Janet Husband.

Statistics are often viewed with considerable scepticism unless they confirm existing conclusions. Relating cancer incidence to possible cause is a sure way of starting discussion. N.E. Day provides a useful analysis of the statistics of cancer occurrence in present day epidemiological research.

Finally, G. P. Murphy and B. W. Girlach review the organizational structures of cancer research, principally in the USA, but with special emphasis on the UICC.

This publication pinpoints some of the most interesting fields in oncology at the present time, but it would not be difficult to a edit a similar supplement in two to three years' time in which such fields as gene transfer, monoclonal antibodies, leukaemia viruses and flow cytometry would perhaps have key roles.

B. W. FOX.

The detection of spinal pseudarthrosis in ankylosing spondylitis

By W. M. Park, M.B., Ch.B., D.M.R.D., F.R.C.R., *D. G. Spencer, M.B., B.S., F.R.A.C.P.,
I. W. McCall, M.B., Ch.B., D.M.R.D., F.R.C.R., D. J. Ward, M.B., Ch.B., F.R.C.P.,
†W. Watson Buchanan, M.D., F.R.C.P. (Glasg. & Edin.) F.R.C.P.(C) and W. H. Stephens, M.D.

The Institute of Orthopaedics, The Robert Jones & Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire, and *The Centre for Rheumatic Diseases, Glasgow

(Received November 1980)

Abstract

Spinal pseudarthrosis in ankylosing spondylitis can be difficult to detect radiologically. This paper assesses the value of bone radioscintigraphy in relation to radiological examination.

The patterns of tracer uptake in the spine were recorded in 16 patients in whom established ankylosing spondylitis was complicated by pseudarthrosis. Twenty such lesions were identified in 16 patients, mostly occurring at one level in a junctional region of the spine. Four patients had two lesions. Standard radiography failed to demonstrate this abnormality in seven patients and in these, tomography was required to confirm the scintigraphic findings.

On the other hand, bone scanning was much less accurate in detecting the minor forms of marginal vertebral end plate destruction (spondylo-discitis) than conventional radiology.

This study suggests that $^{99}Tc^{m}MDP$ scanning is a useful primary investigation for the detection of spinal pseudarthrosis in patients with chronic ankylosing spondylitis who suffer late onset back pain.

The severity of spinal symptomatology in ankylosing spondylitis tends to diminish as intervertebral ossification progresses. The presence of back pain, thereafter, may herald complications such as fracture and pseudarthrosis. These may be difficult to detect radiologically and have occasionally been mistaken for osteomyelitis. The purpose of this presentation is to examine the value of special radiographic techniques and bone scintigraphy in patients who develop pseudarthrosis in long-established ankylosing spondylitis.

Source of Clinical Material

Patients with pseudarthrosis were selected from two main sources: the first, from a combined clinical and radiological survey of 200 patients with ankylosing spondylitis (Spencer *et al.*, 1979). This was done in order to obtain an overall perspective of the incidence of significant findings. The second source was from patients with long-established ankylosing spondylitis who were referred to a rheumatological outpatient clinic and could therefore give an indication of the clinical significance of the problem. As it turned out, all the patients in this group had had the disease over 10 years and this helped to make the radiological discrimination of vertebral end plate lesions more distinct.

The two sources produced a total of 16 patients for consideration in this communication.

Clinical Findings

Only patients with clearly established ankylosing spondylitis by accepted clinical and radiological criteria were included in the study. There were ten males and six females. The age of onset of disease ranged from 13 to 35 years, the average being 23.3 years. The disease duration ranged from ten to 35 years with an average of 22.8 years. The erythrocyte sedimentation rate ranged from 18 to 94 mm in the first hour (Westergren); the average was 54. Back pain was the main presenting symptom in all the patients except one, who is in the incidence survey of the 200-patient group. In ten patients, the back pain represented a recurrence of symptomatology after the disease had been quiescent for a long period. Six patients suffered grumbling backache symptoms from the onset of disease, with exacerbations culminating ultimately in referral to hospital. The symptoms were so severe in three patients with pseudarthrosis that surgical stabilization had to be performed.

Radiological Findings

Extensive intervertebral ankylosis was present in 13 patients with the classical radiological appearances of "bamboo" spine. The remainder demonstrated typical radiological appearances of ankylosing spondylitis in a less complete form.

Two types of radiological disc space abnormality were identified. The first is confined to the vertebral bodies and is classified as spondylo-discitis. The second is associated with a complete transverse segment defect through the disc space and posterior elements and is classified as a pseudarthrosis.

The changes of spondylo-discitis cover a wide spectrum. These range from minor anterior marginal erosion to more extensive vertebral end plate destruction (Fig. 1). These usually occur at multiple levels and 24 were recorded in ten patients.

---

*Present address: Specialist Medical Centre, 151-155 Hawkesbury Road, Westmead NSW 2145, Australia.

†Present address: Department of Rheumatology, Basic Medical Health Sciences, McMaster University, Hamilton, Ontario, Canada.

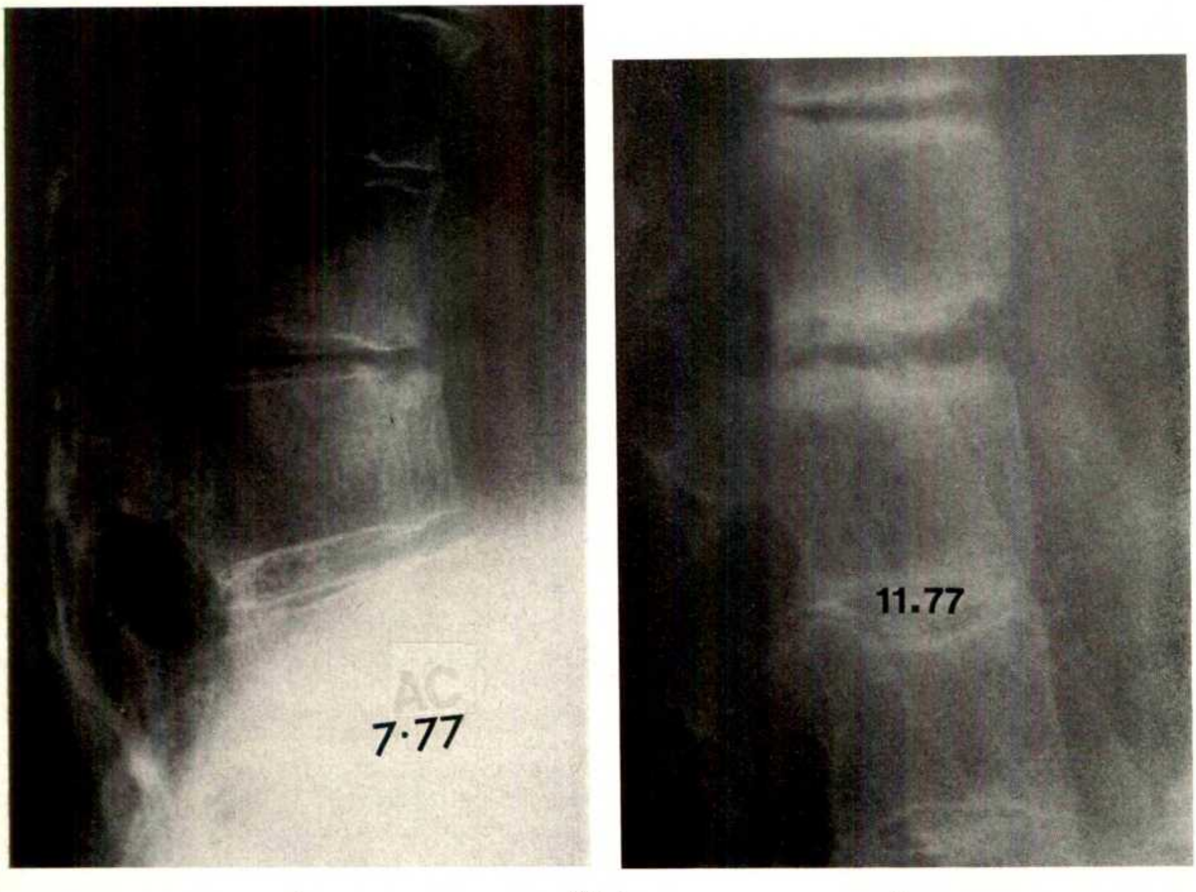
The radiological demonstration of pseudarthrosis was more difficult. Only nine were found to have characteristic appearances which could be confidently interpreted on standard radiographs. These showed gross disc space and vertebral body changes with irregular widening and destruction and a clear posterior defect (Fig. 2). In these patients supplementary lateral radiographs in flexion and extension showed abnormal pivotal movement. Tomography was not performed routinely in all patients. In six, however, the presence of abnormal radioscintigraphy prompted this further investigation and revealed six more examples.

This produced a total of 15 patients with radiologically established pseudarthrosis. In one further patient a radioisotope scan characteristic of pseudarthrosis was found. A complete transverse defect could not be demonstrated radiologically.

The distribution of pseudarthrosis was confined to junctional regions of the spine: the dorsi-lumbar area (D8–L2) was implicated in ten patients, the lumbosacral (L4–S1) in six patients and the cervico-dorsal region (C6–D1) in three. Four patients had lesions at two levels, producing a total of 19 lesions in 15 patients.

Scintigraphic Findings

Bone scans were performed using ^{99}Tc^{m}MDP and abnormal uptake was demonstrated in each patient. Abnormal isotope retention projected over the spinal region in patients with ankylosing spondylitis may be due to a number of causes.



A Fig. 1. B

Spondylo-discitis—dorsal spine. (A) Marginal—the anterior segment of the disc is involved with localized destruction of the opposing vertebral plates and narrowing of the disc space. (B) Complete—there is involvement of the whole vertebral plate, at two levels accompanied by reactive, sclerotic change in the vertebral bodies.

In patients with extensive bony ankylosis producing the radiological appearance of "bamboo" spine, the radioisotope scan is relatively featureless and without the morphological detail which identifies individual spinal segmental anatomy. Thus the contours of the vertebral bodies, spinous processes and apophyseal joints become blurred with intervertebral ossification.

In pseudarthrosis, increased isotope retention occurs in the bones on either side of the transverse defect. Figure 3 illustrates an example of the type of appearances which can be identified in established pseudarthrosis. Four patients had scintigraphic evidence of pseudarthrosis involving two separate spinal segments. In the 16 patients included in this survey therefore, a total of 20 scintigraphic pseudarthrosis examples were found. Nineteen of these were confirmed by the radiographic demonstration of a complete transverse defect and in some instances this required tomography. In the twentieth example of scintigraphic pseudarthrosis, X-ray examination revealed extensive vertebral end plate destruction without a definite fracture of the posterior elements.

In comparison with the isotope appearances in pseudarthrosis, the findings in spondylo-discitis were much more variable and correlated very badly with the radiological appearances. This was particularly true for the partial vertebral plate erosion which is most commonly situated in the anterior half of the vertebra. Radioisotope scanning revealed uptake activity of a lesser degree and different characteristics and manifested by a much more focal appearance. Twelve examples of this type of lesion were recorded in the 16 patients. These were found

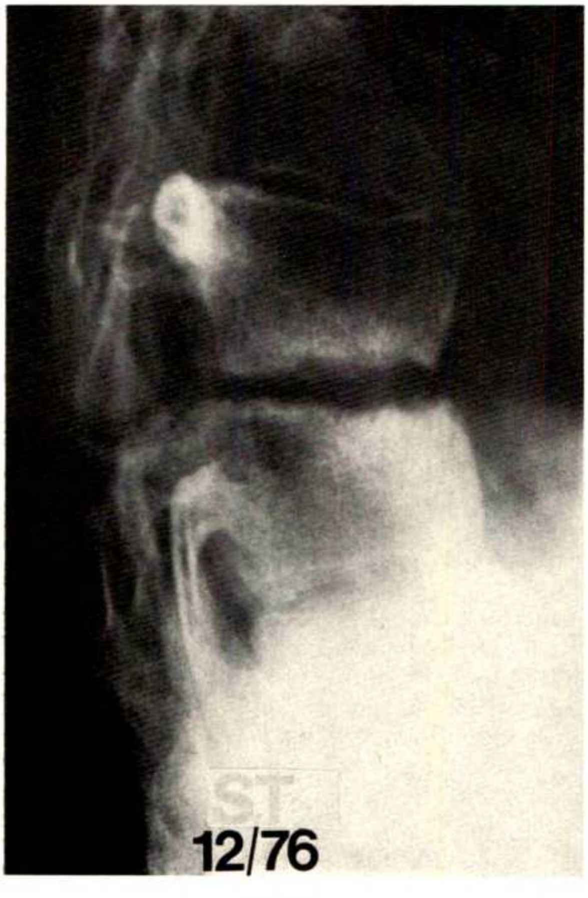


FIG. 2.

Pseudarthrosis—dorsi-lumbar junction. A complete transverse defect has been produced in an ankylosed segment of lower dorsal spine. The vertebral plates show irregular destruction and reactive sclerosis. Pivotal movement occurred through the corresponding apophyseal joint.

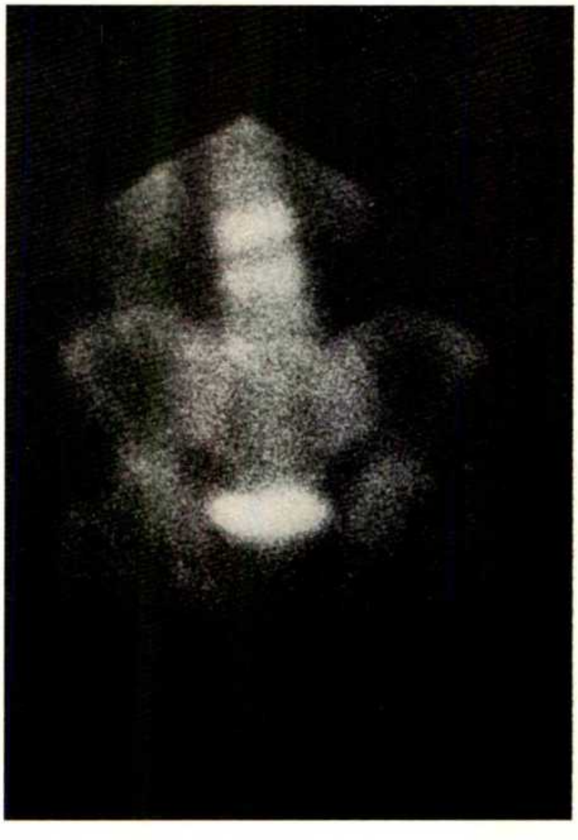


FIG. 3.

Scintigraphic appearances of pseudarthrosis. The isotope tracer is retained within the vertebral bodies on either side of the pseudarthrosis. The complete transverse defect is well shown and serves to differentiate this condition from pyogenic infection.

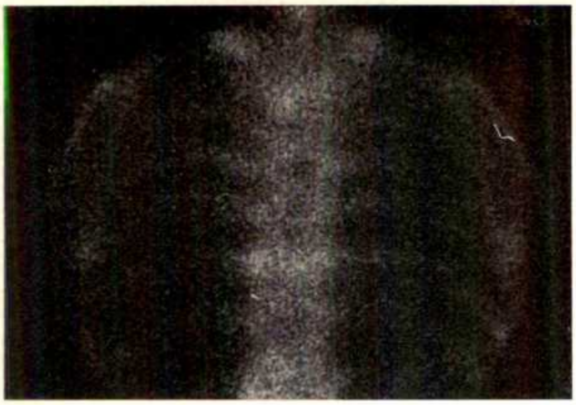


FIG. 4.

Scintigraphic features of focal inflammatory lesions. There is localized tracer retention in costo-transverse, apophyseal joints and spinous processes.

to correlate with the marginal type of spondylo-discitis on the radiographs. However, scintigraphy failed to identify 12 additional identical X-ray abnormalities.

There were eight examples of the complete type of spondylo-discitis lesion and the radioisotope abnormalities ranged between the features characteristic of the anterior marginal defect and established pseudarthrosis.

Areas of abnormal tracer retention were also observed in the vertebral appendages (Fig. 4). These included the apophyseal and costo-vertebral joints (14 levels), spinous processes (seven levels) and the sterno-clavicular joint in one patient.

DISCUSSION

The scintigraphic features of ankylosing spondylitis have been the subject of considerable attention. Scanning technique and methods of quantitation of sacro-iliac involvement for the early diagnosis of disease have been described (Russell *et al.*, 1975; Lentle *et al.*, 1977; Namey *et al.*, 1977; Goldberg *et al.*, 1978). In the spine, early stage disease manifests diffuse isotope uptake which subsequently becomes localized in apophyseal joints, costo-vertebral joints, sterno-clavicular joints or spinous processes. Progression to the stage which gives the radiological appearance of "bamboo" spine results in loss of detailed segmental scintigraphic morphology and isotope activity regresses. It is at this point that identification of focal areas of increased isotope retention becomes important. In a prospective study of 63 patients with ankylosing spondylitis, Lentle *et al.* (1977) found evidence of "focal sterile discitis" in five patients, two of whom were unsuspected until scanned. Only subsequently were these confirmed by tomography.

The present study indicates that abnormal spinal isotope retention can occur in spondylo-discitis and pseudarthrosis. The pattern of uptake appears to be consistent when the latter is associated with considerable end plate destruction of the type seen in severe spondylo-discitis. There was good correlation between scintigraphic activity and complete radiological transverse defects in 15 patients.

Radiographically, these lesions corresponded to the types of pseudarthrosis previously described by Seaman and Wells (1961), Rivelis and Freiberger (1969), Jacobs (1972), Frank and Gleeson (1975), Yau and Chan (1974) and Martel (1978). Scintigraphic features of pseudarthrosis were recorded in one further patient and although radiographically severe vertebral end plate destruction was present a posterior arch defect could not be demonstrated despite the use of tomography. Since this lesion was asymptomatic, it is possible that it could represent either an incipient or even possibly a healing posterior arch fracture. In the other patients, scintigraphic evidence of pseudarthrosis correlated well with spinal pain symptomatology.

In marked contrast with these findings, significantly lower isotope retention was observed in the minor forms of marginal spondylo-discitis. These are usually situated in the anterior margins of the vertebrae and correspond to those described by Romanus and Yden (1952). Radiological examination revealed 24 levels affected by this type of lesion but only 50% were demonstrable by scintigraphy. There was no correlation between clinical symptomatology and the presence of these radiological lesions. It is possible, therefore, that the isotopic appearances represent minor localized inflammatory effects but without discriminant radiographic features. These findings are similar to those of Little *et al.* (1974), who observed asymptomatic spondylo-discitis in six patients with long-standing ankylosing spondylitis.

The incidence of these mild and severe forms of spondylo-discitis is quite different. Review of 200 patients (Spencer *et al.*, 1979) showed evidence of mild inflammatory spondylo-discitis in 53%. This is comparable to the findings of Dihlmann and Delling (1978) who observed these lesions in 31 out of 58 patients. Severe destructive vertebral lesions and pseudarthrosis are much less common. Schultz (1968) found a 6% incidence of severe vertebral plate destructive lesions in patients with disease duration greater than ten years. This compares with

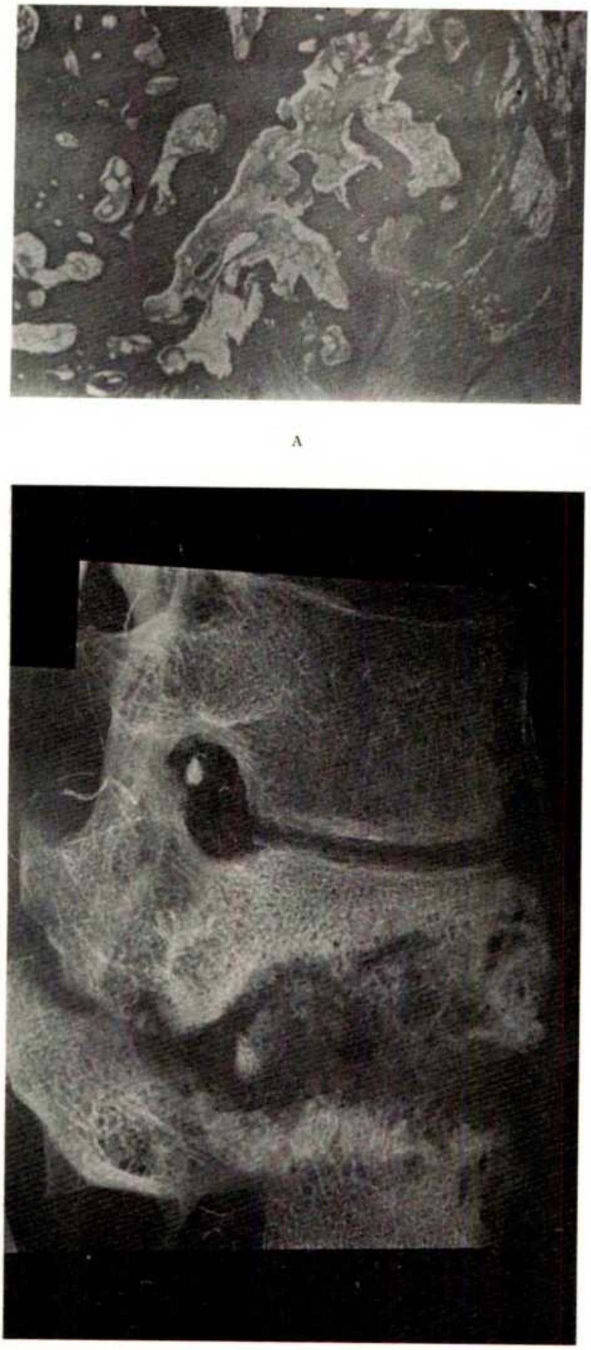


FIG. 5.

Pseudarthrosis of L1–2 level—cadaveric specimen. (A) Histological findings: the necrotic bone spicules throughout the field show empty lacunae. Whorls of fibrous callus are present on the right. (B) Radiological findings: there is extensive destruction of both vertebral bodies with complete absence of the end plate. The transverse defect extends across the apophyseal joint, whilst the one above remains ankylosed.

our review series which revealed an incidence of destructive vertebral lesions of 4%, and in 2.5% this was associated with pseudarthrosis and fracture.

The histological appearances of inflammatory vertebral lesions in early stage disease have previously been well recorded (Baggenstoss *et al.*, 1952; Wholey *et al.*, 1960; Sutherland and Matheson, 1974). The predominant feature is the presence of granulomatous tissue invading bone through defects in the intervertebral plate.

The sequence of events in pseudarthrosis is not absolutely clear, but it has been suggested by Cawley *et al.* (1972) that fracture of the posterior elements may not heal. Continued movement at that spinal level may ultimately produce a segmental pseudarthrosis. The histological findings are characteristic and represented by fibrous callus and necrotic bone spicules (Fig. 5). However, it could equally be argued that a severe degree of vertebral end plate destruction permits an excessive degree of mobility producing fracture through ankylosed apophyseal joints.

In either event, from a management point of view it is clearly important to recognize these lesions so that appropriate immobilization and supportive therapy can be commenced. In the majority of patients in this series the painful symptoms could be controlled with simple measures. However, three patients did require surgical fusion because of uncontrollable pain. No neurological complications have been recorded in this series. But spinal cord compression has been reported following lesions at the dorsi-lumbar junction (Lorber *et al.*, 1961; Kanefield *et al.*, 1969; Good, 1967; Hansen *et al.*, 1967; Rapp and Kernek, 1974).

The value of ^{99}Tc^{m} in the detection of pseudarthrosis in other conditions was questioned. Using this technique, Hannon *et al.* (1977) reported a number of failures in detecting pseudarthrosis following spinal fusion for scoliosis. This may be partly due to technical limitations in obtaining optimum resolution in deep structures in the presence of severe spinal deformity. It is possible that the inflammatory spondylo-discitis of ankylosing spondylitis augments bone response which, in some way, enhances isotope retention.

In conclusion, the presence of back pain in late stage ankylosing spondylitis should alert the clinician to the possibility of developing fracture or pseudarthrosis. There should be an increased index of suspicion when the disease has previously been clinically quiescent. The evidence provided by this study would suggest that radioscintigraphy may be regarded as a valuable primary investigation which will detect significant lesions and particularly pseudarthrosis with a high degree of accuracy.

REFERENCES

BAGGENSTOSS, A. H., BICKEL, W. H. and WARD, L. E., 1952. Rheumatoid granulomatous nodules as destructive lesions of vertebrae. *Journal of Bone & Joint Surgery*, 34-*A*, 601–609.

CAWLEY, M. I. D., CHALMERS, T. M., KELLGREN, J. H. and BALL, J., 1972. Destructive lesions of vertebral bodies in ankylosing spondylitis. *Annals of Rheumatic Diseases, 31*, 345–358.

DIHLMANN, W. and DELLING, G., 1978. Disco-vertebral destructive lesions (so-called Andersson lesions) associated with ankylosing spondylitis. *Skeletal Radiology, 3*, 10–16.

FRANK, P. and GLEESON, J. A., 1975. Destructive vertebral lesions in ankylosing spondylitis. *British Journal of Radiology, 48*, 755–758.

GOLDBERG, R. P., GENANT, H. K., SHIMSHAK, R. and SHAMES, D., 1978. Applications and limitations of quantitative sacroiliac joint scintigraphy. *Radiology, 128*, 683–686.

GOOD, A. E., 1967. Non-traumatic fracture of the thoracic spine in ankylosing spondylitis. *Arthritis & Rheumatism, 10*, 467–469.

HANNON, K. M. and WETTA, W. J., 1977. Failures of Tc bone scanning to detect pseudarthrosis in spinal fusion for scoliosis. *Clinical Orthopaedics, 123*, 42–44.

HANSEN, S. T., TAYLOR, T. K. F., HONET, J. C. and LEWIS, F. R., 1967. Fracture-dislocations of the ankylosed thoracic spine in rheumatoid spondylitis. *The Journal of Trauma, 7*, 827–837.

JACOBS, P., 1972. Some uncommon manifestations of ankylosing spondylitis. *Proceedings of the Second Congress of the European Association of Radiology* (Excerpta Medica, Amsterdam) pp.211–217.

KANEFIELD, D. G., MULLINS, B. P., FREEHAFER, A. A., FUREY, J. G., HORENSTEIN, S. and CHAMBERLIN, W. B., 1969. Destructive lesions of the spine in rheumatoid ankylosing spondylitis. *Journal of Bone and Joint Surgery, 51-A*, 1369–1375.

LENTLE, B. C., RUSSELL, A. S., PERCY, J. S. and JACKSON, F. I., 1977. The scintigraphic investigation of sacroiliac disease. *Journal of Nuclear Medicine, 18*, 529–533.

LITTLE, H., UROWITZ, M. B., SMYTHE, H. A. and ROSEN, P. S., 1974. Asymptomatic spondylo-discitis. An unusual feature of ankylosing spondylitis. *Arthritis & Rheumatism, 17*, 487–493.

LORBER, A., PEARSON, C. M. and RENE, R. M., 1961. Osteolytic vertebral lesions as a manifestation of R. A. and related disorders. *Arthritis & Rheumatism, 4*, 514–531.

MARTEL, W., 1978. Spinal pseudarthrosis. A complication of ankylosing spondylitis. *Arthritis & Rheumatism, 21*, 485–490.

NAMEY, T. C., MCINTYRE, J., BUSE, M. and LEROY, E. C., 1977. Nucleographic studies of axial spondarthritides. I. Quantitative sacroiliac scintigraphy in early HLA–B27 associated sacroiliitis. *Arthritis & Rheumatism, 20*, 1058–1064.

RAPP, G. F. and KERNEK, C. B., 1974. Spontaneous fracture of the lumbar spine with correction of deformity in ankylosing spondylitis. *Journal of Bone & Joint Surgery, 56–A*, 1277–1278.

RIVELIS, M. and FREIBERGER, R. H., 1969. Vertebral destruction at unfused segments in late ankylosing spondylitis. *Radiology, 93*, 251–256.

ROMANUS, R. and YDEN, S., 1952. Destructive and ossifying spondylitic changes in rheumatoid ankylosing spondylitis. *Acta Orthopaedica Scandinavica, 22*, 88–99.

RUSSELL, A. S., LENTLE, B. C. and PERCY, J. S., 1975. Investigation of sacroiliac disease. Comparative evaluation of radiological and radionuclide techniques. *Journal of Rheumatology, 2*, 45–51.

SCHULTZ, K. P., 1968. Destruktive Veränderungen an Wirbelkörpern bei der Spondylarthritis ankylopoetica. *Archiv für Orthopädische und Unfall-Chirurgie, 64*, 116–134.

SEAMAN, W. B. and WELLS, J., 1961. Destructive lesions of the vertebral bodies in rheumatoid disease. *American Journal of Roentgenology, 86*, 241–250.

SPENCER, D. G., PARK, W. M., DICK, H. M., PAPAZOGLOU, S. N. and BUCHANAN, W. W., 1979. Radiological manifestations in 200 patients with ankylosing spondylitis: correlation with clinical features and HLA B27. *Journal of Rheumatology, 6*, 305–315.

SUTHERLAND, R. I. L. and MATHESON, D., 1974. Mechanisms of vertebral destruction in ankylosing spondylitis. *Arthritis & Rheumatism, 17*, 502.

WHOLEY, M. H., PUGH, D. G. and BICKEL, W. H., 1960. Localized destructive lesions in rheumatoid spondylitis. *Radiology, 74*, 54–56.

YAU, A. C. M. C. and CHAN, R. N. W., 1974. Stress fracture of the fused lumbo-dorsal spine in ankylosing spondylitis. *Journal of Bone & Joint Surgery, 56–B*, 681–687.

1981, *British Journal of Radiology*, *54*, 473–478

JUNE 1981

Juvenile hyaline fibromatosis

By D. A. Stringer and C. M. Hall

Radiology Department, Hospital for Sick Children, Great Ormond Street, London WC1

(*Received November 1980*)

ABSTRACT

A case of juvenile hyaline fibromatosis in a ten-year-old Asian girl is presented. This autosomal recessively inherited condition has not previously been described in the radiological literature. This patient demonstrates well the characteristic radiological appearance. The literature of juvenile hyaline fibromatosis and of the other generalized fibromatoses is reviewed and the interrelationship is discussed.

In his classic review of 44 cases of childhood fibromatoses, Stout (1954) established the existence of congenital generalized fibromatosis and described it as "congenital multinodular tumour formation involving superficial and muscular tissues as well as viscera and bones". He described two cases which had visceral involvement, one of which had a solitary bone involved—the upper femur.

Schnitka *et al.* (1958) described a further case with full autopsy findings which had 53 soft tissue tumours, the largest being 4.5 cm and expanding but not destroying the right orbit.

Since then there have been sporadic reports in the literature. The first report of generalized fibromatosis in the radiological literature was from Condon and Allen (1961) who showed lobulated, well defined, occasionally slightly expanded, radiolucent lesions in long and flat bones which had little if any marginal sclerosis. This patient was reported elsewhere by Beatty (1962).

A radiological review by Morettin *et al.* (1972) of 21 cases of generalized fibromatosis showed that nine of these 21 cases had bone involvement, five of these dying before four months of age, one partially remitting and three showing complete spontaneous remission. The radiological findings were similar to those reported by Condon and Allen (1961), but they found that symmetrical eccentric metaphyseal involvement, more often medial than lateral, was characteristic. One patient with skull vault involvement by extrinsic pressure was mentioned. Their own patient showed a diaphyseal periosteal reaction involving the long bones of all extremities. Spinal involvement was common but often was not appreciated except at autopsy. Lung involvement was occasionally present and appeared identical to interstitial fibrosis or generalized bronchopneumonia.

This review did not mention the patients of Puretic *et al.* (1962), Ishikawa and Hori (1964) and Drescher *et al.* (1967), none of which fitted into the histological classification of Stout. Puretic *et al.* (1962) reported a "unique form of mesenchymal dysplasia". They reported osteolysis of the distal phalanges at the age of six-and-a-half years which progressed to nearly complete lysis of the distal phalanges within three years. Ishikawa and Hori (1964) described a cortical defect in the medial aspect of the proximal tibial shaft in his patient. Drescher *et al.* (1967) described two siblings where the histology showed an abundance of homogeneous, amorphous, acidophilic ground substance containing spindle-shaped cells forming minute streaks. This differed from the histology described by Stout, as did the clinical history, and they suggested that it was a distinct condition which could be called "fibromatosis hyalinica multiplex juvenalis". The histology and electron microscopic findings on this patient were described by Woyke *et al.* (1970).

Enjoji *et al.* (1968) reported two further siblings with scalp tumours, but no radiological abnormality was seen in these. Later in 1972 Kitano *et al.* reported two siblings with a similar condition which they called "Juvenile hyaline fibromatosis". In their search of the world literature they found nine other cases. These included the patients of Puretic *et al.* (1962), Ishikawa and Hori (1964), Drescher *et al.* (1967) and Enjoji *et al.* (1968), but also included three patients described by Murray (1873) as "peculiar cases of molluscum fibrosum".

Gutierrez *et al.* (1973) have described a further example which had distal phalangeal destruction similar to that seen by Puretic *et al.* but also had a round translucent lesion in the left ankle.

Kitano (1976) reported a patient with destruction of the proximal humerus with absent humeral heads, and translucent lesions in the left femur and left tibia. He reported also that one of his previous cases had developed a punched-out osteolytic lesion in the skull at the age of 12 years and that this was followed by destruction of humeral heads and distal phalanges.

CASE REPORT

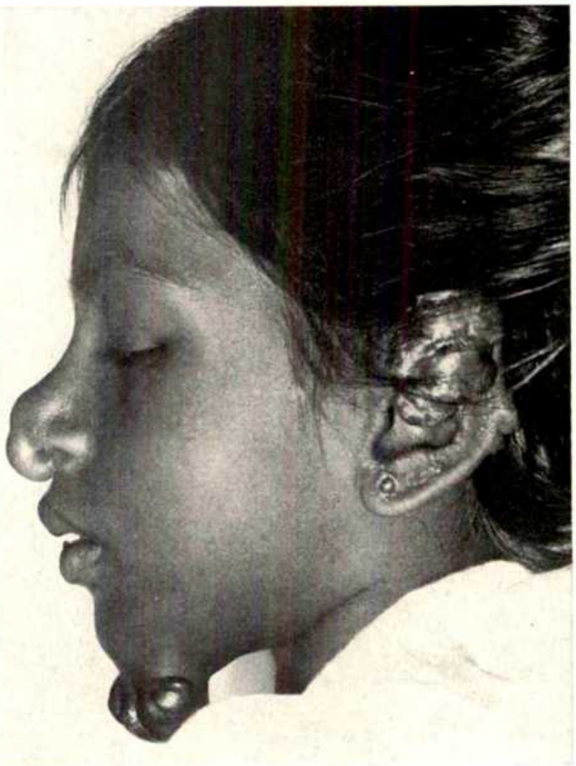
The patient is a ten-year-old girl, the second child of healthy unrelated Kenyan Indian parents. Her 16-year-old brother is healthy. She was born by normal delivery and appeared well until the age of two years, when she developed cutaneous swellings in the scalp. These swellings gradually enlarged and at the time of first attendance at The Hospital for Sick Children, Great Ormond Street, at the age of six years, they were present over the face and ears (Fig. 1), back and left inguinal region. They all appeared fluctuant with a variable degree of fixation to deep structures. The skull radiograph (Fig. 2) showed the soft tissue masses but no bony abnormality.

The hands and feet showed multiple swellings of the terminal phalanges of the fingers and toes (Fig. 3). Radiographs of the hands and feet taken at a later date showed severe acro-osteolysis (Fig. 4) with expanded lytic lesions in the distal phalanges of both big toes. Soft tissue swelling was associated with the acro-osteolysis.

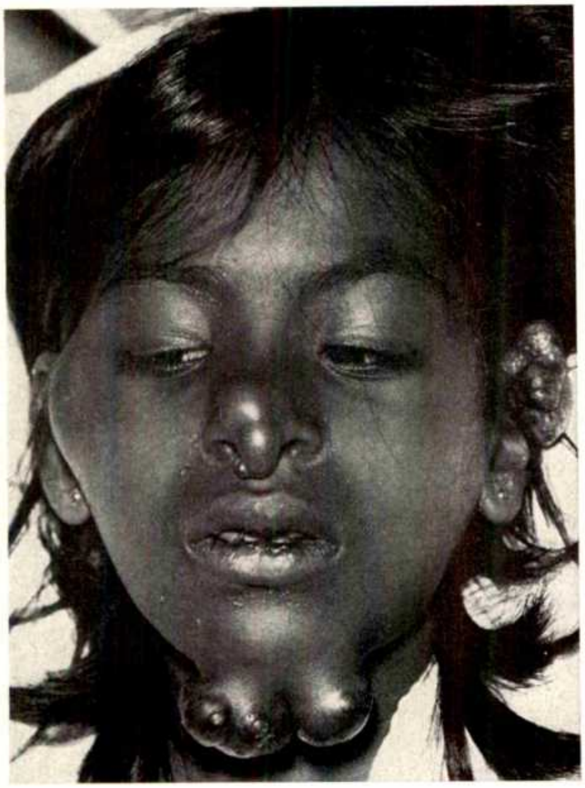
A skeletal survey showed slender long bones with relatively large epiphyses and coxa valga. There were abnormalities of the left ankle, both knees and left elbow. The left ankle showed a well demarcated translucency with a thin sclerotic rim on the medial margin of the lateral malleolus (Fig. 5). The knees showed symmetrical well-demarcated defects at the proximal ends of both tibiae medially (Fig. 6). The left elbow showed a well-demarcated translucent lesion with a thin sclerotic rim in the distal end of the humerus (Fig. 7).

There were hard subcutaneous lumps in the palms and hard areas over the lower borders of the axillae spreading round on to the scapulae. Flexion of the right knee was limited to 90° due to pain. There was widespread lymphadenopathy especially in the neck, submandibular and axillary regions. Overlying the thoracic spine were two soft swellings. No neurological deficit was present. The chest was clear, heart sounds were normal and no abdominal abnormality was found.

Excision biopsy of the chin lumps was performed and the histology showed mostly acellular PAS positive matrix containing a certain amount of collagen. It had a hyaline appearance, but Congo Red and Thioflavine T stains for



B



A

FIG. 1.

Frontal (A) and lateral (B) aspect of patient's head showing subcutaneous masses on chin, nose and left ear.

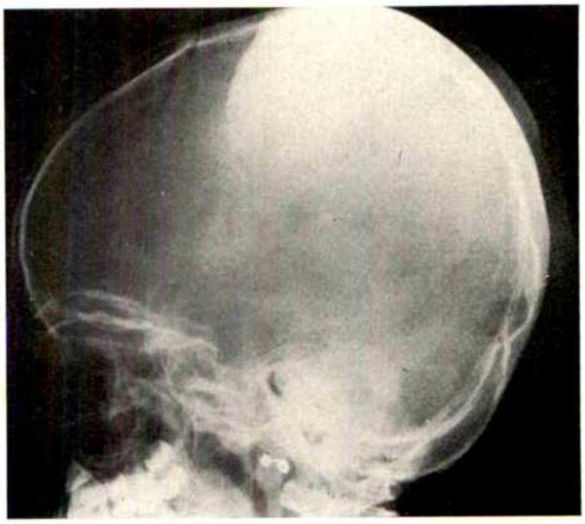
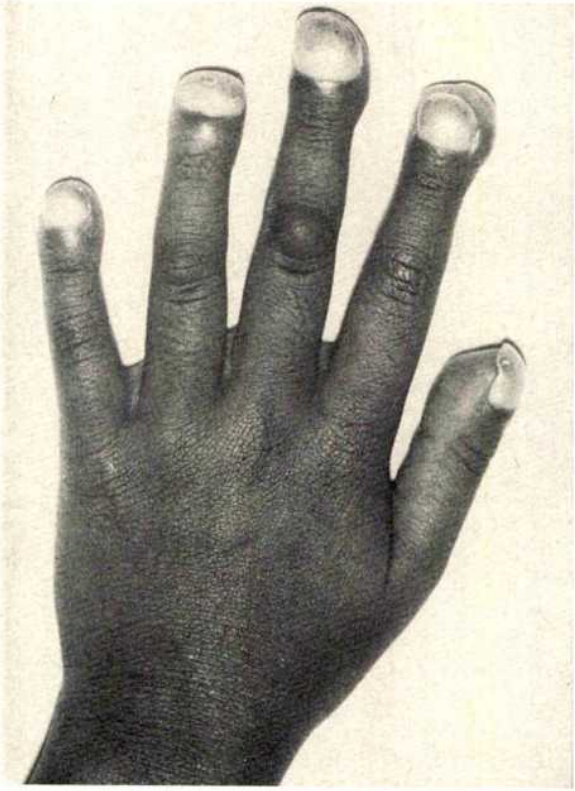
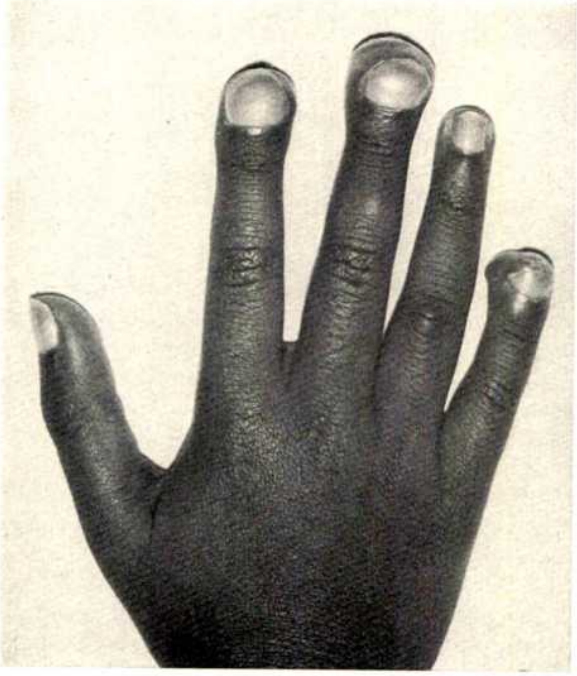


FIG. 2.

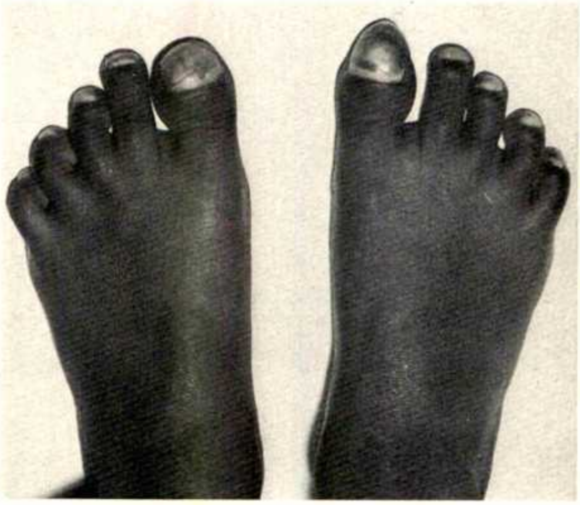
Lateral skull radiograph showing soft tissue density masses overlying occipital and parietal regions



A



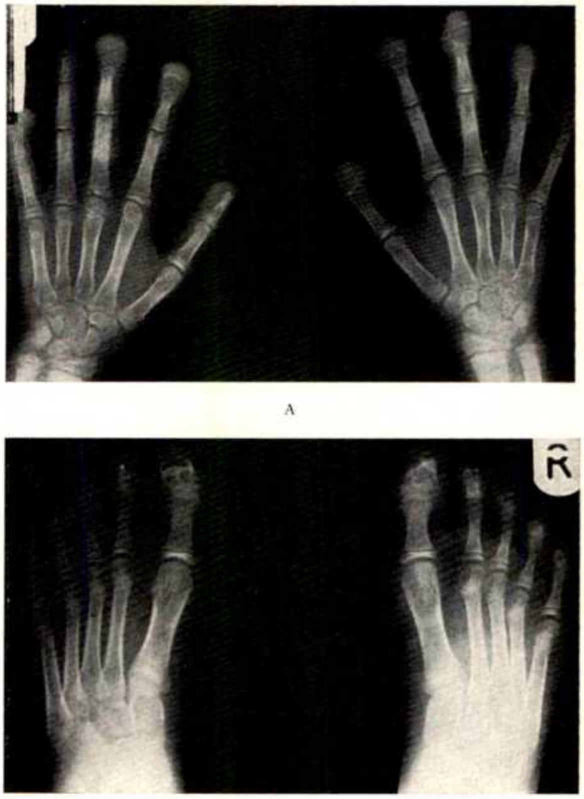
B



C

FIG. 3.

Hands and feet showing multiple swelling of fingers and toes.



A

B

FIG. 4.

PA radiograph of both hands and DP radiograph of both feet showing marked acro-osteolysis with associated soft tissue swelling. There is a well demarcated translucency within the distal phalanx of each hallux.

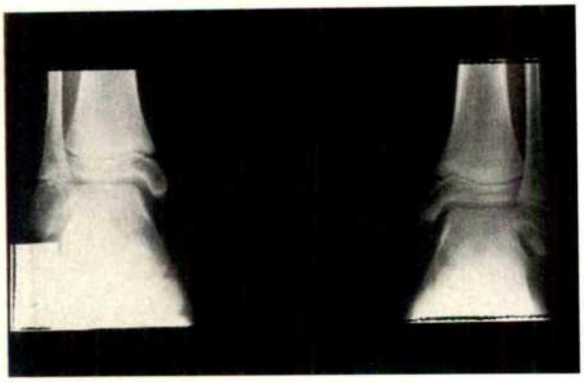


FIG. 5.

AP radiograph of both ankles showing disparity in size between the diaphysis and epiphysis with a translucent defect in the left distal fibular epiphysis.

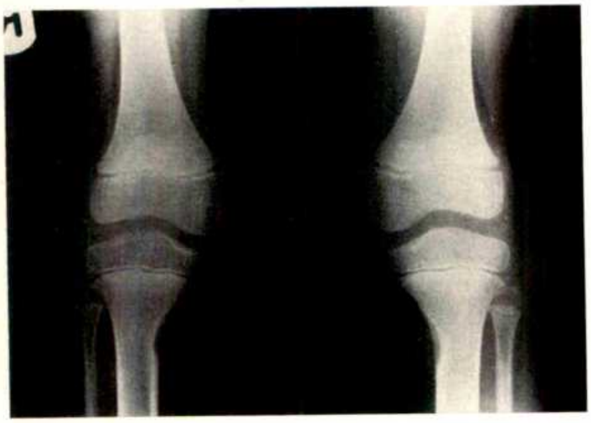


FIG. 6.

AP radiograph of both knees showing slender diaphyses, slightly enlarged epiphyses and translucent defects in the medial aspects of both upper tibiae.

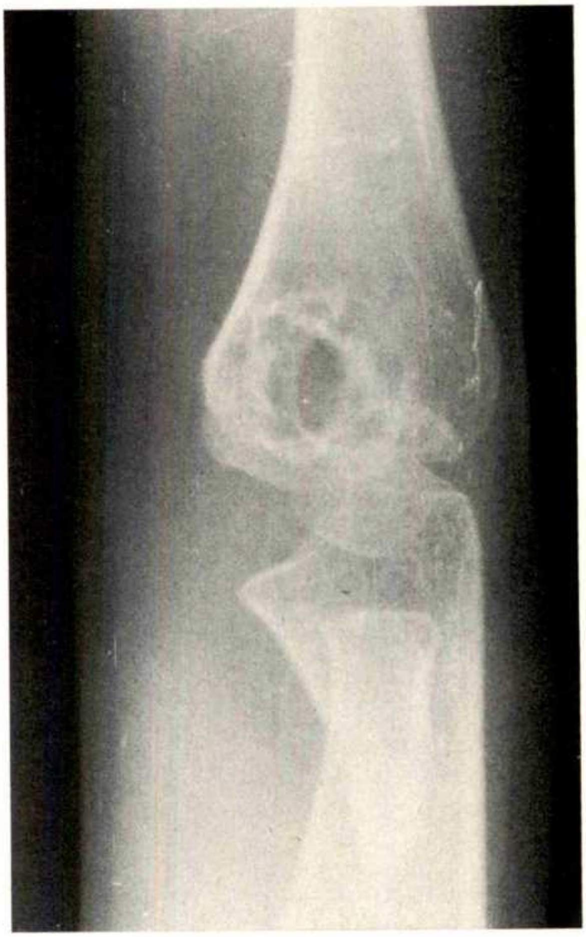


FIG. 7.

Oblique radiograph of the left elbow demonstrating a translucency with a sclerotic margin in the distal humerus.

amyloid were negative. The included fibroblasts were plump but no pleomorphism or mitoses were seen. The lesion showed some areas of vascularity. The features were compatible with juvenile hyaline fibromatosis.

She was readmitted four more times for cosmetic excisions of her lumps and on the third of these she complained of a little rectal bleeding. Sigmoidoscopy appeared normal but a biopsy showed hyaline deposits. Similar histology was found on a biopsy of her gingiva which was hyperplastic. A double-contrast enema on her last admission was normal.

DISCUSSION

Juvenile hyaline fibromatosis was not included in MacKenzie's excellent review (1972) of the histological classification of fibromatoses. Puretic *et al.* had called it a mesenchymal dysplasia, and Drescher, fibromatosis hyalinica multiplex juvenalis, but it was only later that Kitano *et al.* firmly established it as a separate condition and reviewed the past literature. MacKenzie has reclassified the fibromatoses since 1972 (Table I) (personal communication, 1980). He has included hyaline fibromatosis but feels that this inclusion is debatable because it does not share some of the features common to all the other fibromatoses.

Including the present patient, there have been 13 patients described with this condition. Juvenile hyaline fibromatosis differs histologically and clinically from generalized fibromatosis and it has a distinctive radiological appearance as discussed below.

Juvenile hyaline fibromatosis is a rare condition presenting with skin lumps between two months and four years of age, unlike generalized fibromatosis which usually presents at birth with skin nodules. In

TABLE I

THE FIBROMATOSES

Congenital, infantile and juvenile fibromatoses	Fibrous hamartoma of infancy Fibromatosis colli Digital fibrous tumour of infancy Juvenile aponeurotic fibroma Congenital generalized fibromatosis Juvenile hyaline fibromatosis Hereditary gingival fibromatosis Miscellaneous fibromatoses
Adult fibromatoses	Palmar and plantar fibromatoses Mesenteric fibromatoses Musculoaponeurotic fibromatoses Generalized fibromatoses

Morettin *et al.*'s review of generalized fibromatosis, five of their 21 definite cases presented at birth, and all except two had presented by one month of age. These two patients presented at three months and 49 years respectively. In view of the remarkable age of presentation of this last patient the histology was reviewed by Stout and the diagnosis of generalized fibromatosis was confirmed (Geschickter, 1955).

The present case presented at the age of two years with cutaneous swellings of the scalp and face. Nine of the previous 12 patients reported had scalp lumps, all being quite large except for the case of Ishikawa and Hori who found smaller subcutaneous nodules. Generalized fibromatosis frequently gives subcutaneous nodules and these are common in the head and neck so this is not a useful differentiating feature.

By the age of six years, when first seen at the Hospital for Sick Children, Great Ormond Street, these scalp and face masses were very large. Smaller masses were present on the back and inguinal region. The masses in generalized fibromatosis have also been reported over the back and inguinal region and in many other areas.

Kitano reported a punched-out osteolytic lesion in the skull vault which was found for the first time during the follow-up of one of his patients with juvenile hyaline fibromatosis when the patient was over 12 years of age. Our patient, like the other 11 patients, did not have any osseous skull lesions. It is of interest that Teng *et al.* (1963) described extrinsic pressure erosion of the vault in one case of generalized fibromatosis which was subsequently included in Morettin *et al.*'s review.

The most marked radiological abnormality in our patient with juvenile hyaline fibromatosis is the gross acro-osteolysis with expanded translucent lesions in the distal phalanges of hands and feet which appeared at five years. A similar finding was described by Puretic *et al.*, whose male patient developed the acro-osteolysis at seven years of age. Gutierrez (1973) also reported destruction of a distal phalanx. One of the patients described by Kitano in 1972 later developed acro-osteolysis when he was over 12 years old (Kitano, 1976). Acro-osteolysis has not been described in generalized fibromatosis.

This patient of Kitano's also developed destruction of both humeral heads giving a striking radiological appearance. Kitano also found this appearance in a new patient whom he described at the same time (1976). Neither our patient nor any of the other ten cases showed humeral head destruction. Our patient showed slender long bones and relatively large epiphyses which affected the humeral heads to the same extent as the other epiphyses. There was a minor coxa valga deformity. The large epiphyses, slender shafts and coxa valga have not been reported previously.

The cortical defects in the proximal shafts of the tibiae medially have been previously described by Ishikawa and Hori (1964). These were present but less prominent in our patient and not described in the other 11 patients.

There are three reports of bone lucencies in the 13 patients with juvenile hyaline fibromatosis. Gutierrez showed a round translucency in the ankle. "Punched-out osteolytic lesions in the femur and tibia" were reported by Kitano (1976), but not illustrated in his article. Our case showed well-demarcated translucent lesions with a thin sclerotic rim seen in the left distal humerus and left lateral malleolus. A strikingly similar abnormality has been found in generalized fibromatosis and was described by Condon and Allen. This was also found in nine of the 21 definite cases of Morettin *et al.* (1972).

In our case, flexion of the right knee was limited to 90° due to pain. This is unlike four of the previous 12 cases, all males, which showed flexural contractures with limitation of extension of a number of joints including the knee (Puretic *et al.*, 1962; Ishikawa and Hori, 1964; Kitano *et al.*, 1972). This was felt by Kitano to be due to infiltration of the joints by tumour tissue. Flexural contractures were not described in Morettin's review of generalized fibromatosis.

No neurological abnormality has been found in this condition and all cases described have been of normal intelligence.

Twelve of the 14 had gingival hypertrophy, including the present patient, in which gingival biopsy showed the histological appearance similar to the tumours biopsied. The presence or absence of gingival hypertrophy was not commented on in the other two patients. Gingival hypertrophy is not a feature of generalized fibromatosis.

Rectal bleeding and the finding of infiltration of the large bowel by hyaline deposits has not been reported previously.

The previous reports favour a recessive mode of inheritance but there was no family history of consanguinity in our patient.

Ten of the 21 definite cases of generalized fibromatosis reviewed by Morettin died before four months of age, nine dying under two-and-a-half months of age. Of the other 11, the outcome of two was unknown, four spontaneously regressed and three regressed after surgery with no recurrence. Two were known to be living and well some time after the diagnosis but full information was not available. This poor initial prognosis has not been seen in juvenile hyaline fibromatosis, the major morbidity being due to flexural contractures. There has been only one death in the 11 recently reported patients—a six-year-old male who had high fever on three occasions culminating in jaundice, acute dyspnoea and finally death (Kitano *et al.*, 1972). The autopsy showed that fulminant hepatitis and oedema of the brain were the direct cause of death. Infiltration of amorphous eosinophilic substance was found in the tongue, oesophagus, stomach, intestine, thymus, spleen and lymph nodes. The muscles of he extremities were infiltrated with fatty tissue.

Juvenile hyaline fibromatosis is a rare mesenchymal abnormality which may be differentiated from other generalized fibromatoses. All these conditions present in childhood, often with multiple subcutaneous tumours, which commonly occur on the head and neck and with well-demarcated translucencies in the metaphyses of long bones. However juvenile hyaline fibromatosis has a later age of presentation and a better prognosis. The presence of flexural contractures favours a diagnosis of juvenile hyaline fibromatosis. Juvenile hyaline fibromatosis is associated with marked gingival hypertrophy and sometimes has characteristic gross acro-osteolysis with or without humeral head destruction.

ACKNOWLEDGMENTS

We would like to thank Professor D. H. MacKenzie from the Department of Histopathology at Westminster Hospital for kindly providing his modified table of fibromatoses and for his helpful comments. We would also like to thank Mrs. Gill Porter for cheerfully typing the manuscript and its corrections.

REFERENCES

Beatty, E. C., 1962. Congenital generalised fibromatosis in infancy. *Americal Journal of Diseases of Children, 103*, 620–624.

Condon, V. R. and Allen, R. P., 1961. Congenital generalised fibromatosis: case report with roentgen manifestations. *Radiology*, *76*, 444–448.

Drescher, E., Wyke, S., Markeiwicz, C. and Tegi, S., 1967. Juvenile fibromatosis in siblings (fibromatosis hyalinica multiplex juvenalis). *Journal of Pediatric Surgery*, *2*, 427–430.

Enjoji, M., Kato, S., Kamikozuru, K. and Arima, E., 1968. Juvenile fibromatosis of the scalp in siblings. *Acta Medica University of Kagoshima, 10 (Supplement)*, 145–151.

Geschickter, C. F., 1955. Desmofibromatosis and viscerofibromatosis. *Bulletin of Georgetown University Medical Centre*, *8*, 200–206.

Gutierrez, G., Zambrano, V., Garcia, F., Martin, F., Ospina, J. and Camargo, H., 1973. Fibromatosis hialinica multiple juvenil, a proposito de un caso. *Medicina Cutanea*, *7*, 283–286.

Ishikawa, H. and Hori, Y., 1964. Systematisierte Hyalinose in Zusammenhang mit Epidermolysis bullosa polydystrophica und Hyalinosis cutis et mucosae. *Archiv für Klinische und Experimentelle Dermatologie*, *218*, 30–51.

Kitano, Y., Hoshiki, M., Aoki, T. and Sagami, S., 1972. Two cases of juvenile hyaline fibromatosis. *Archives of Dermatology*, *106*, 877–883.

Kitano, Y., 1976. Juvenile hyaline fibromatosis. *Archives of Dermatology*, *112*, 86–88.

MacKenzie, D. H., 1972. The fibromatoses, a clinicopathological concept. *British Medical Journal, iv*, 277–281.

Morettin, L. B., Muller, E. and Schreiber, M., 1972. Generalised hamartomatosis (congenital generalised fibromatosis). *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *114*, 722–734.

Murray, J., 1873. On three peculiar cases of molluscum fibrosum in children. *Medico-Chirurgical Transactions*, *38*, 235–253.

Puretic, S., Puretic, B., Fiser-Herman, M. and Adamcic, M., 1962. A unique form of mesenchymal dysplasia. *British Journal of Dermatology*, *74*, 8–19.

Schnitka, R. K., Asp, D. M. and Horner, H. R., 1958. Congenital generalised fibromatosis. *Cancer*, *11*, 627–639.

Stout, A. P., 1954. Juvenile fibromatosis. *Cancer*, *7*, 953–978.

Teng, P., Warden, M. J. and Cohn, W. L., 1963. Congenital generalised fibromatosis (renal and skeletal) with complete spontaneous regression. *Journal of Pediatrics*, *62*, 748–753.

Woyke, S., Domagala, W. and Olszewski, W., 1970. Ultrastructure of a fibromatosis hyalinica multiplex juvenilis. *Cancer*, *26*, 1157–1168.

1981, *British Journal of Radiology*, *54*, 479–483

JUNE 1981

Renal function after high dose urography in patients with renal failure

By *Judith A. W. Webb, M.R.C.P., F.R.C.R., *R. H. Reznek, M.R.C.P., F.R.C.R.,
†W. R. Cattell, M.D., F.R.C.P. and *I. Kelsey Fry, D.M., F.R.C.P., F.R.C.R.

Departments of *Diagnostic Radiology and †Nephrology, St. Bartholomew's Hospital, London EC1A 7BE

(*Received December 1980*)

ABSTRACT

A retrospective study of 40 patients with moderate to severe renal failure who had high dose urography showed that none developed oliguric acute renal failure after the urogram. In 37 patients there was no worsening in renal function attributable to the urogram This group included five patients in whom renal function was already deteriorating at the time of the urogram. In three patients a transient rise in serum creatinine without oliguria occurred in the week following urography. Differences between the British and North American experience are discussed.

In the late 1960's high dose urography using approximately twice the usual dose of contrast medium was introduced for patients with renal failure. The early reported series suggested that there were few harmful effects on renal function (Bengtsson *et al.*, 1968; Bartley *et al.*, 1969; Fulton *et al.*, 1969; Mahaffy *et al.*, 1969; Brown *et al.*, 1970; Davidson *et al.*, 1970; Fry and Cattell, 1971). The few reports of renal failure after urography were largely in patients who had been dehydrated before the urogram (Bergman *et al.*, 1968; Gross *et al.*, 1968; Pillay *et al.*, 1970; Dudzinski *et al.*, 1971; Barshay *et al.*, 1973; Feldman *et al.*, 1974; Agarwal *et al.*, 1975; Diaz-Buxo *et al.*, 1975; Light and Hill, 1975; Matz *et al.*, 1975) and high dose urography in renal failure was accepted as a useful and relatively safe procedure (Grainger, 1972). More recently there has been a dramatic proliferation in the American literature of reports of acute renal failure (ARF) after a number of contrast medium procedures, including high dose urography (Ansari and Baldwin, 1976; Harkonen and Kjellstrand, 1977; Kamdar *et al.*, 1977; Alexander *et al.*, 1978; Carvallo *et al.*, 1978; Cohen *et al.*, 1978; Krumlovsky *et al.*, 1978; Shafi *et al.*, 1978; van Zee *et al.*, 1978; Vesely and Mintz, 1978; Weinrauch *et al.*, 1978; Byrd and Sherman, 1979; Older, 1979) (Fig. 1). In the week following urography these patients developed a substantial rise in serum creatinine (greater than 0.27 mmol/l), accompanied in the majority by transient oliguria. In some patients the renal failure was sufficiently severe to necessitate dialysis (Ansari and Baldwin, 1976; Harkonen and Kjellstrand, 1977; van Zee *et al.*, 1978) and in a few it was irreversible (Harkonen and Kjellstrand, 1977; Weinrauch *et al.*, 1978). In many patients hydration did not appear to protect against the development of acute renal failure.

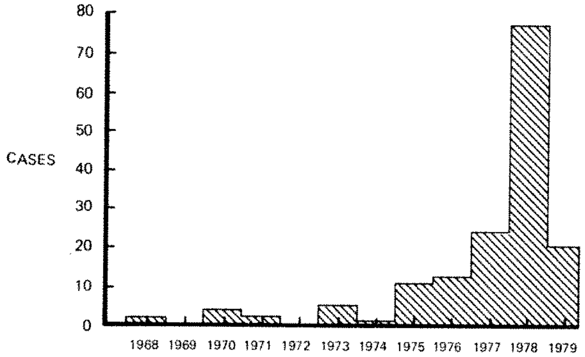


FIG. 1.

Reported cases of acute renal failure after intravenous urography, 1968–1979.

In our hospital high dose urography in renal failure has been performed frequently over the past 13 years but we had not been aware of this sequence of events having occurred in any of our patients. Further we have not seen this problem in the many referrals of patients in renal failure from other hospitals to our Regional Dialysis Unit. Nonetheless the reported frequency and severity of this complication led us to make a detailed retrospective study of renal function in our patients before and after high dose urography.

PATIENTS AND METHODS

Only those patients with renal failure (serum creatinine <0.18 mmol/l) referred from the Renal Unit for high dose urography were studied, as these were likely to have renal function particularly well documented before and after the urogram. The notes were available for 165 of 186 patients referred for high dose urography between 1973 and 1979.

The criteria for inclusion in the study were, first that patients were not undergoing dialysis at the time of the urogram as this would make it impossible to evaluate renal function and, second, that adequate data on renal function before and after urography were available. These consisted preferably of at least one serum creatinine in the week before and two in the week after the urogram, together with a serum creatinine at one month after the urogram. Failing this, serial blood ureas had to be available. 100 patients were excluded because of dialysis at the time of the urogram and a further 25 because the available data were inadequate.

In the 40 patients with well-documented renal failure, serum creatinine, blood urea and 24-hour urine volumes in the week before and after the urogram were recorded. In the majority more than the minimum acceptable number were available (two or more values before the urogram in 34 patients, and three or more after the urogram in 36 patients). The patient's age and the cause of the renal failure were noted. Any factors that might be relevant to deterioration of renal function such as exposure to nephrotoxic drugs, or episodes of hypotension, were specifically sought.

The urographic technique used in all cases was identical. The patients were hydrated at the time of the urogram and care was taken to ensure that their metabolic and cardiovascular state was optimal. A dose of 600 mg I/kg of sodium diatrizoate (Hypaque 45) was given by slow intravenous injection over several minutes. On the basis of our laboratory's experience of serum creatinine estimation in the range studied we regarded a change in serum creatinine of 12% between two readings as significant.

The patients' ages ranged from 10–72 years with majority (75%) under the age of 60. There was a wide range of causes of renal failure among the patients (Table I). Two of the 40 patients had diabetes mellitus.

TABLE I

Aetiology of renal failure

Aetiology	No. of cases
Obstructive uropathy	6
Chronic renal failure, cause not known	5
Chronic glomerulonephritis	3
Atherosclerotic vascular disease and/or hypertension	3
Septicaemia	3
Gout	2
Amyloid	2
Wegener's granulomatosis	2
Acute glomerulonephritis	2
Acute tubular necrosis*	2
Systemic vasculitis ?PAN	1
Analgesic nephropathy	1
Calculus disease	1
Diabetic nephropathy	1
Systemic lupus erythematosus	1
Neurogenic bladder	1
Polycystic disease of kidneys	1
Acute suppurative pyelonephritis	1
Microangiopathic haemolytic anaemia	1
Methadone overdose	1

*One of these patients had diabetes mellitus.

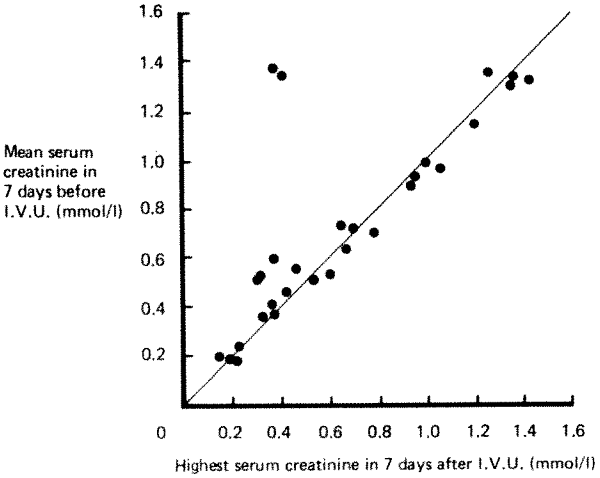


Fig. 2.

Relation of mean serum creatinine in the week before the urogram to the highest serum creatinine in the week after the urogram.

Results

None of the 40 patients developed acute oliguric renal failure. Thirty-seven patients showed no deterioration in renal failure attributable to the urogram. In 32, there was no worsening in renal function after the urogram. In 29 of these, when the mean serum creatinine in the week before the urogram was compared with the highest value in the week after the urogram, there was no significant increase in serum creatinine (Fig. 2). In two patients there was no increase in the blood urea in the week following the urogram. In one further patient who had dialysis to the day of the urogram, the serum creatinine subsequently remained stable for two days and then fell. In the remaining five of the 37 patients in whom the urogram produced no deterioration of renal function, renal function was already worsening at the time of the urogram. In this group the serum creatinine was rising before the urogram but there was no acceleration of this rise when contrast medium was given, nor was there oliguria (Fig. 3).

In three patients there was a transient rise in serum creatinine in the week following the urogram (Fig. 4). In one diabetic woman with acute tubular necrosis after an episode of dehydration the serum creatinine rose from the mean of the previous week's values by 23% (0.195 mmol/l) on the day after the urogram but then fell rapidly. In two patients with chronic renal failure the serum creatinine rose from

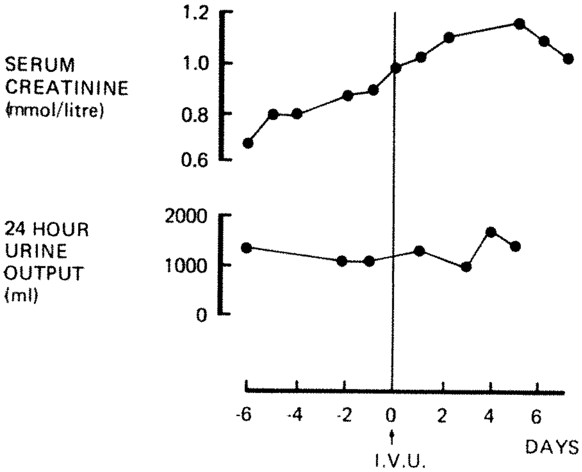


FIG. 3.

Example of a case in which the urogram produced no acceleration in the underlying deterioration of renal function.

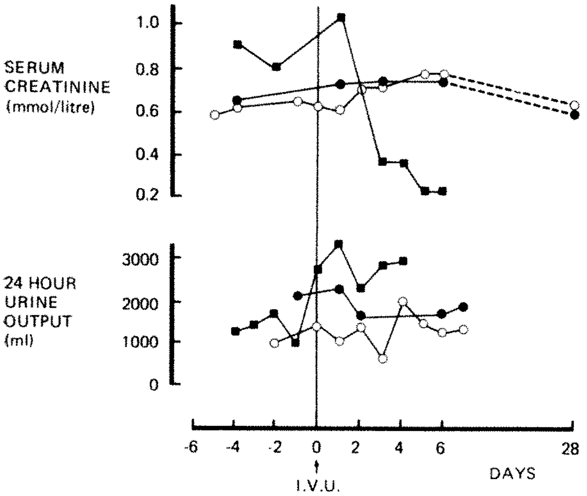


FIG. 4.

Three cases in which there was a transient rise in serum creatinine after the urogram.

the mean of the previous week's values by 16% (0.110 mmol/l) and 27% (0.170 mmol/l) respectively on the sixth day after the urogram, but had fallen to pre-urographic values by the 28th day. In none of these cases was there oliguria and in none was there any other factor such as exposure to nephrotoxic drugs or an episode of hypotension to account for the serum creatinine rise.

DISCUSSION

Renal function has been documented before and after high dose urography in 40 patients with moderate to severe renal failure and in none did oliguria or ARF develop. A transient rise in serum creatinine in three patients probably did represent an adverse but relatively unimportant effect of the contrast medium on renal function. Stage *et al.* (1971) made a similar observation in 17% of their patients in renal failure.

We are aware of the deficiencies associated with any retrospective study. We have rejected 25 cases because of inadequate documentation. In none of these have we reason to believe there was a deterioration of renal function and we do not consider that their exclusion biases our study. Our findings, together with the fact that we provide a Regional Service for the management of ARF, yet have never seen a patient with ARF attributable to urography, indicate that our experience of nephrotoxicity of contrast media after urography differs greatly from that in North America.

To explain this difference we have reviewed the literature, looking for evidence either that the population we investigated differed from the reported cases or that there were significant differences in urographic technique between the two groups.

The severity of renal failure does not appear to be an explanation for the American findings. The majority of our patients had more severe renal failure than did those described in the literature. Our five patients in whom renal function was already worsening at the time of urography are particularly interesting. Any adverse effect of contrast medium would be expected to be particularly evident in this group, yet none was observed. No cases of this type were described in the American series. It is possible that a failure to recognise that renal function was deteriorating before the urogram explains the apparently harmful effect of contrast medium in some of the reported cases.

The range of aetiologies in our patients was similar to those in the American series with the important exception that the number of diabetics in our series was small. Seventy-nine of the 163 reported cases (49%) of ARF after urography occurred in diabetics. Diabetic patients in renal failure appear to be a particular risk from high dose urography (Bergman *et al.*, 1968; Pillay *et al.*, 1970; Barshay *et al.*, 1973; Feldman *et al.*, 1974; Agarwal *et al.*, 1975; Diaz-Buxo *et al.*, 1975; Matz *et al.*, 1975; Ansari and Baldwin, 1976; Harkonen and Kjellstrand, 1977; Kamdar *et al.*, 1977; Alexander *et al.*, 1978; Carvallo *et al.*, 1978; Cohen *et al.*, 1978; Krumlovsky *et al.*, 1978; Shafi *et al.*, 1978; van Zee *et al.*, 1978; Vesely and Mintz, 1978; Weinrauch *et al.*, 1978; Byrd and Sherman, 1979). The explanation for this is as yet unclear, but this susceptibility to renal failure does not appear to apply to diabetics with normal renal function (Harkonen and Kjellstrand, 1979).

Elderly patients also appear to be more at risk of developing acute renal failure after high dose urography. 60–80% of patients in the various reported series were over the age of 60, as compared with only 23% of our cases.

Preparation for the urogram appears to be important: 67 of the 163 reported cases were fluid restricted or dehydrated before urography (Bergman *et al.*, 1968; Gross *et al.*, 1968; Pillay *et al.*, 1970; Dudzinski *et al.*, 1971; Barshay *et al.*, 1973; Feldman *et al.*, 1974; Agarwal *et al.*, 1975; Diaz-Buxo *et al.*, 1975; Light and Hill, 1975; Matz *et al.*, 1975; Ansari and Baldwin, 1976; Harkonen and Kjelstrand, 1977; Kamdar *et al.*, 1977; Alexander *et al.*, 1978; Cohen *et al.*, 1978; Carvallo *et al.*, 1978; Krumlovsky *et al.*, 1978; van Zee *et al.*, 1978; Weinrauch *et al.*, 1978; Byrd and Sherman, 1979; Older, 1979). Equally, however, it is clear that hydration alone does not protect patients from developing ARF. We believe that our practice of ensuring that our patients are in an optimal metabolic and cardiovascular condition before the urogram is very important in preventing the development of ARF.

Many of the American patients received a larger dose of contrast medium than did our patients. Sixty-four of the 138 cases reported since 1976 were given 300 ml of 30% sodium diatrizoate as a standard dose (Ansari and Baldwin, 1976; Harkonen and Kjellstrand, 1977; Shafi *et al.*, 1978; van Zee *et al.*, 1978). This gives 600 mg I/kg to a 90 kg patient, but all patients smaller than this would receive a proportionately larger dose. This contrasts with our practice of using a strictly weight-related dose of 600 mg I/kg. Repeated contrast medium procedures over a short time interval also appear to increase the risk of ARF. Twenty of the 138 cases reported since 1976 had more than one procedure in fairly rapid succession (Ansari and Baldwin, 1976; Alexander *et al.*, 1978; Cohen *et al.*, 1978; Byrd and Sherman, 1979).

Since a vascular aetiology has been suggested for the ARF produced by contrast medium (Byrd and Sherman, 1979) it was thought possible that a faster injection of contrast might predispose to this complication. This does not appear to be the case on the available evidence: our patients received their contrast by a bolus injection over several minutes while the majority of the American patients were given theirs by an intravenous infusion (Ansari and Baldwin, 1976; Harkonen and Kjellstrand, 1977; Shafi *et al.*, 1978; van Zee *et al.*, 1978).

TABLE II

RISK FACTORS FOR THE DEVELOPMENT OF ACUTE RENAL FAILURE AFTER HIGH DOSE UROGRAPHY

1	Diabetes mellitus
2	Dehydration or fluid restriction before the urogram
3	Large contrast medium dose
4	Repeated contrast procedures in a short period of time
5	Age over 60 years

No single factor has been found to account for the occurrence of ARF in the American patients. Further elucidation of this will almost certainly require a very large and carefully conducted prospective study. Nonetheless a number of risk factors can be identified (Table II). These must be borne in mind during the selection and preparation of patients, and during the performance of high-dose urography in patients with impaired renal function, especially now that the technique is used so widely.

REFERENCES

Agarwal, B. N., Cabebe, F. and McCormick, C., 1975. Renal effects of urography in diabetes mellitus. *Annals of Internal Medicine*, *83*, 902.

Alexander, R. D., Berkes, S. L. and Abuelo, J. G., 1978. Contrast media-induced oliguric renal failure. *Archives of Internal Medicine*, *138*, 381–384.

Ansari, Z. and Baldwin, D. S., 1976. Acute renal failure due to radio-contrast agents. *Nephron*, *17*, 28–40.

Barshay, M. E., Kaye, J. H., Goldman, R. and Coburn, J. W., 1973. Acute renal failure in diabetic patients after intravenous infusion pyelography. *Clinical Nephrology*, *1*, 35–39.

Bartley, O., Bengtsson, U. and Cederbom, G., 1969. Renal function before and after urography and angiography with large doses of contrast media. *Acta Radiologia Diagnostica*, *8*, 9–16.

Bengtsson, U., Cederbom, G., Falkheden, T. and Jagenburg, R., 1968. Clearances of inulin and para-aminohippurate before and after urography using high dosage of contrast medium in patients with renal insufficiency. *Scandinavian Journal of Urology and Nephrology*, *2*, 173–176.

Bergman, L. A., Ellison, M. R. and Dunea, G., 1968. Acute renal failure after drip-infusion pyelography. *New England Journal of Medicine*, *279*, 1277.

Brown, C. B., Glancy, J. J., Fry, I. K. and Cattell, W. R., 1970. High-dose excretion urography in oliguric renal failure. *Lancet*, ii, 952–955.

Byrd, L. and Sherman, R. L., 1979. Radiocontrast-induced acute renal failure. *Medicine*, *58*, 270–279.

Carvallo, A., Rakowski, T. A., Argy, W. P. and Schreiner G. E., 1978. Acute renal failure following drip infusion pyelography. *American Journal of Medicine*, *65*, 38–45.

Cohen, M., Meyers, A. M., Milne, F. J., Disler, P. B. and Van Blerk, P. J. P., 1978. Acute renal failure after use of radiographic contrast media. *South African Medical Journal*, *54*, 662–664.

Davidson, A. J., Becker, J., Rothfield, N., Unger, G. and

Ploch, D. R., 1970. An evaluation of the effect of high-dose urography on previously impaired hepatic and renal function in man. *Radiology, 97*, 249–254.

Diaz-Buxo, J. A., Wagoner, R. D., Hattery, R. R. and Palumbo, P. J., 1975. Acute renal failure after excretory urography in diabetic patients. *Annals of Internal Medicine, 83*, 155–158.

Dudzinski, P. J., Petrone, A. F., Persoff, M. and Callaghan, E. E., 1971. Acute renal failure following high dose excretory urography in dehydrated patients. *Journal of Urology, 106*, 619–621.

Feldman, H. A., Goldfarb, S. and McCurdy, D. K., 1974. Recurrent radiographic dye-induced acute renal failure. *Journal of the American Medical Association, 229*, 72.

Fry, I. K. and Cattell, W. R., 1971. Excretion urography in advanced renal failure. *British Journal of Radiology, 44*, 198–202.

Fulton, R. E., Witten, D. M. and Wagoner, R. D., 1969. Intravenous urography in renal insufficiency. *American Journal of Roentgenology, 106*, 623–634.

Grainger, R. G., 1972. Renal toxicity of radiological contrast media. *British Medical Bulletin, 28*, 191–195.

Gross, M., McDonald, H. and Waterhouse, K., 1968. Anuria following urography with meglumine diatrizoate (Renografin) in multiple myeloma. *Radiology, 90*, 780–781.

Harkonen, S. and Kjellstrand, C. M., 1977. Exacerbation of diabetic renal failure following intravenous pyelography. *American Journal of Medicine, 63*, 939–946.

1979. Intravenous pyelography in non-uremic diabetic patients. *Nephron, 24*, 268–270.

Kamdar, A., Weidmann, P., Makoff, D. L. and Massry, S. G., 1977. Acute renal failure following intravenous use of radiographic contrast dyes in patients with diabetes mellitus. *Diabetes, 26*, 643–649.

Krumlovsky, F. A., Simon, N., Santhanam, S., del Greco, F., Roxe, D. and Pomaranc, M. M., 1978. Acute renal failure. Association with administration of radiographic contrast material. *Journal of the American Medical Association, 239*, 125–127.

Light, J. A. and Hill, G. S., 1975. Acute tubular necrosis in a renal transplant recipient. *Journal of the American Medical Association, 232*, 1267–1268.

Mahaffy, R. G., Mattheson, N. A. and Caridis, D. T., 1969. Infusion pyelography in acute renal failure. *Clinical Radiology, 20*, 320–323.

Matz, R., Camacho, F., Sable, R. and Seinfeld, D., 1975. Renal effects of urography in diabetes mellitus. *Annals of Internal Medicine, 83*, 902.

Older, R., 1979. Contrast-induced renal failure: a radiological problem and a radiological diagnosis. *Radiology, 131*, 553–554.

Pillay, V. K. G., Robbins, P. C., Schwartz, F. D. and Kark, R. M., 1970. Acute renal failure following intravenous urography in patients with long-standing diabetes mellitus and azotaemia. *Radiology, 95*, 633–636.

Shafi, T., Chou, S. Y., Porush, J. G. and Shapiro, W. B., 1978. Infusion intravenous pyelography and renal function. *Archives of Internal Medicine, 138*, 1218–1221.

Stage, P., Brix, E., Folke, K. and Karle, A., 1971. Urography in renal failure. *Acta Radiologica Diagnostica, 11*, 337–345.

Van Zee, B. E., Hoy, W. E., Talley, T. E. and Jaenike, J. R., 1978. Renal injury associated with intravenous pyelography in non-diabetic and diabetic patients. *Annals of Internal Medicine, 89*, 51–54.

Vesely, D. L. and Mintz, D. H., 1978. Acute renal failure in insulin-dependent diabetics: episodes secondary to intravenous pyelography. *Archives of Internal Medicine, 138*, 1858–1859.

Weinrauch, L. A., Robertson, W. S. and D'Elia, J. A., 1978. Contrast media-induced acute renal failure. *Journal of the American Medical Association, 239*, 2018–2019.

Book review

Endoscopic Retrograde Cholangio-pancreatography. Ed. by T. Takemoto and K. Kasugai, pp. x+328, 1979 (Igaku-Shoin, Tokyo/New York), $61.00.
ISBN 0-89640-027-1

Endoscopic retrograde cholangio-pancreatography originated in Japan, and this is the first major Japanese publication available in the English language. The editors are well known for their major contributions in the field, and they have invited a galaxy of Japanese stars. The first few chapters concern the history of the technique, methods of duodenoscopy, and possible complications. Unfortunately, the technical descriptions are not designed to give much guidance to the beginner who has difficulty in finding the papilla and cannulating it; nor is much space devoted to the clinical role of diagnostic ERCP—indeed the chapter on indications and contra-indications consists of a single page. Of great interest are two chapters concerning the correlations between pancreatic duct morphology and exocrine function. The data from Kozu has not appeared previously, and is pertinent to clinical practice.

These chapters are followed by those concerning extensions of ERCP-studies on pure pancreatic juice, methods of endoscopic sphincterotomy for stone removal, and the latest techniques of per-oral pancreatico-choliangoscopy, using baby fibrescopes. Nakamura then discusses choledochoscopy, including his unique experience of using fibrescopes down the post-operative T-tube track.

The second half of the book is more specifically radiological, with descriptions and illustrations of the endoscopic and radiographic findings in different pancreatic and biliary diseases. Many of the radiographs are accompanied by illustrative case reports. These again emphasize the concentration on ERCP, and give little guidance as to its developing relationships with other imaging techniques, such as ultrasound and CT scanning.

The book is well presented, with excellent reproduction of the radiographs, and with high quality colour endoscopic and histological illustrations. Extensive references are given with most chapters, but very few are later than 1976.

All groups interested in ERCP and its ramifications will wish to have access to this book.

P. B. Cotton.

1981, *British Journal of Radiology*, *54*, 484–487

The effect of DDAVP on intravenous urography

By *A. K. Dixon, M.A., M.R.C.P., F.R.C.R., Judith A. W. Webb, B.Sc., M.R.C.P., F.R.C.R.,
W. R. Cattell, M.D., F.R.C.P. and I. Kelsey Fry, D.M., F.R.C.P., F.R.C.R.

Departments of Diagnostic Radiology and Nephrology, St. Bartholomew's Hospital, London EC1A 7BE

(*Received January 1981*)

ABSTRACT

The possible role of an antidiuretic hormone analogue, DDAVP (1 deamino-8-*D*-arginine vasopressin), in intravenous urography has been studied. The minimum effective dose of intravenous DDAVP in normal hydrated subjects was shown to be 2 ng/kg. During intravenous urography in fluid restricted subjects, a dose of 1 μg DDAVP was necessary to reduce significantly the urine flow rate after contrast medium injection. Although the mean pyelographic score after DDAVP was increased, the differences observed were not statistically significant. The possible reasons for this finding are discussed.

The radiodensity of the pyelogram obtained during intravenous urography depends on two principal factors—the concentration of contrast medium in the urine and the depth of contrast laden urine through which the X-ray beam passes. The depth of the collecting system depends on its volume, which in turn relates to the anatomy of the system, the rate of urine flow and the effectiveness of the partial ureteric obstruction induced by abdominal compression bands. The concentration of contrast medium in the urine depends on the dose of contrast medium given and the degree to which the glomerular filtrate is concentrated as it passes along the renal tubule (Fry *et al.*, 1967). Since the circulating level of endogenous antidiuretic hormone (ADH) is one of the factors facilitating water reabsorption in the distal renal tubule, it became standard practice to enhance this by fluid restriction of patients before intravenous urography. Some workers took this further by giving exogenous ADH—as pitressin (Wald and Galloway, 1944; Bream, 1957) or lysine vasopressin (Benness, 1970)—before urography. However, these agents have the disadvantage of vasopressor side-effects. The introduction of an ADH analogue, 1-deamino-8-*D*-arginine vasopressin (DDAVP) without pressor side-effects (Vavra *et al.*, 1968; Edwards *et al.*, 1973; Ward and Fraser, 1974) stimulated a study of the possible role of this agent in improving the quality of the intravenous urogram.

DDAVP has a prolonged action, the duration of which relates to the dose given (Andersson *et al.*, 1972). A prolonged antidiuretic effect could be undesirable in patients undergoing intravenous urography. Since the smallest effective dose was not known, a preliminary study in hydrated subjects was undertaken to determine both the minimum effective dose of DDAVP and its duration of action. Our investigations were then extended to determine the effect of three different doses of DDAVP, given before urography, on the contrast induced diuresis and on the quality of the pyelograms. Since we wished to investigate the possible role of DDAVP in normal urographic practice, we elected to study fluid restricted patients and to use abdominal compression bands during urography, although we recognized that both of these measures were likely to diminish the demonstrable effect of DDAVP.

The study was approved by the St. Bartholomew's Hospital Ethical Committee and the informed consent of all subjects and patients was obtained.

METHODS

1. *Minimum effective dose of DDAVP in hydrated subjects*

Based on animal studies (Vavra *et al.*, 1968; Mulder, 1974, personal communication), a dose of DDAVP of 1–2 ng/kg was chosen. Well hydrated volunteers (urine osmolality < 200 mOsm/kg) were given either saline or DDAVP (Ferring) intravenously in a dose of 1 or 2 ng/kg, prepared by serial dilution. They were unaware of which injection they had received. No further fluid was drunk for two hours. Urine samples were obtained before the injection and at 30-minute intervals for two hours. A one litre water load was then given and serial urine collections continued for approximately two further hours. Urine flow rate and osmolality (Advanced Osmometer) were measured on all urine samples. Subjects were asked to record any adverse effects noted.

2. *Effect of DDAVP on intravenous urogram*

Patients requiring intravenous urography for clinical management were studied. The following were excluded: those with elevated serum creatinine or known urinary tract abnormalities, children, patients on diuretics and those unable to tolerate abdominal compression. All patients were fluid restricted before intravenous urography: those who had morning appointments were fluid restricted overnight and those with afternoon appointments had nothing after one cup of fluid at breakfast. Patients emptied their bladder on arrival in the department and again after 30 minutes (urine 1). If the urine flow rate in this period exceeded 0.6 ml/min it was considered that the quality of the intravenous urogram might be improved by DDAVP and these patients were selected for further study.

---

*Present address: University Department of Radiology, Addenbrooke's Hospital, Cambridge.

Intravenous DDAVP or placebo (saline) was given according to a randomizing chart. The dose used initially was 200 ng DDAVP (Group A). Subsequently doses of 1 μg (Group B) and 4 μg (Group C) were used. As the study was spread over more than a year, each dose schedule for DDAVP had its own control group to reduce possible seasonal variation in urine flow rates. Forty minutes after injection of DDAVP the patient again voided (urine 2). An intravenous line was then inserted. Blood was taken for serum creatinine estimation and contrast medium was injected in a dose of 325 mgI/kg (sodium iothalamate, Conray 325). The intravenous urogram was performed according to our standard practice, with exposures at 60–70 kV and ureteric compression applied from five to ten minutes after contrast injection. The patient again voided (urine 3) before the after-micturition film was obtained at approximately 30 minutes. Patients who had received DDAVP were instructed not to drink more than 500 ml over the next three hours, and were asked to report any adverse effects.

Urine flow rate and osmolality (Advanced Osmometer) were measured on all urine samples. Urinary creatinine concentration was measured in urine 1 and serum creatinine on the blood sample. From these the basal creatinine clearance was calculated.

The intravenous urograms were reviewed and those with anatomical abnormalities were excluded. The ten-minute "compression" films were scored by two observers, who did not know whether saline or DDAVP had been given. The upper, middle and lower calyceal groups and pelvis of each kidney were scored by eye on a scale of 0–5—a modification of a previously described method (Fry *et al.*, 1967). The mean of the two observers' scores was obtained, the possible maximum score being 40.

Statistical analysis of the results was by Student's *t* test.

RESULTS

1. *Minimum effective dose of DDAVP*

All subjects showed a rise in urine osmolality during the two hour period of fluid deprivation following the administration of saline or DDAVP (Fig. 1). The increase in osmolality was greater in subjects given DDAVP than in those given saline but in those given 1 ng/kg of DDAVP the difference was only transiently significant at 60 minutes (Table I). By contrast, in subjects given 2 ng/kg of DDAVP, urine osmolalities were significantly higher than those observed in saline treated subjects in all urine samples after the first 30-minute collection.

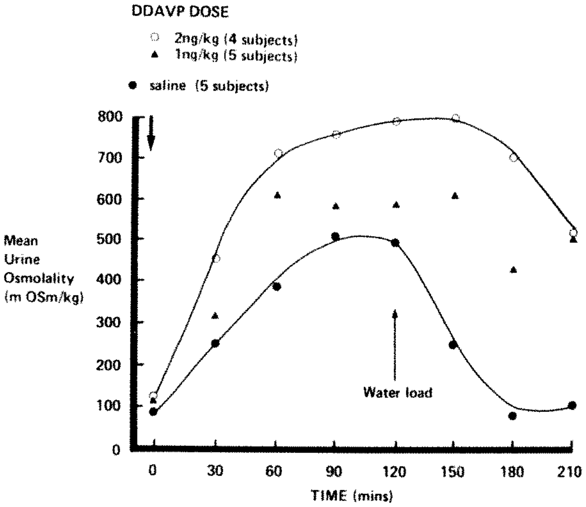


FIG. 1.

The effect of DDAVP on urine osmolality in hydrated subjects.

TABLE I

THE EFFECT OF DDAVP ON URINE OSMOLALITY IN HYDRATED SUBJECTS.

	Time after DDAVP injection (minutes)				
	30	60	90	120	150
DDAVP 1 ng/kg versus saline	NS	< 0.05	NS	NS	< 0.01
DDAVP 2 ng/kg versus saline	NS	< 0.01	< 0.01	< 0.01	< 0.01

Following the water load, urine osmolality fell rapidly in saline treated subjects but fell significantly more slowly in those given DDAVP, remaining above base line levels for at least 3½ hours from the time of administration (Fig. 1; Table I).

No adverse subjective effects of the DDAVP were noted.

2. *Effect of DDAVP on patients undergoing intravenous urography*

Of patients attending for urography approximately 25% had urine flow rates greater than 0.6 ml/min and a total of 85 were entered into the study. Of these, 69 had creatinine clearances greater than 90 ml/min, 12 had creatinine clearances in the 60–90 ml/min range and only four had a clearance of less than 60 ml/min. There was no significant difference in the mean creatinine clearance between DDAVP and saline treated patients in any of the matched groups studied. No patient reported any adverse effect of DDAVP.

(a) *Effect of DDAVP on urine flow rate*

Urine flow rate rather than urine osmolality was studied because interpretation of urinary osmolality values of contrast laden urine would be difficult. The administration of 200 ng of DDAVP resulted in a slightly lower urine flow rate compared with patients given saline (Fig. 2). The difference was not statistically significant. By contrast, in patients given 1 μg or 4 μg of DDAVP, urine flow rate after contrast was significantly lower than in control patients.

(b) *Effect of DDAVP on pyelogram quality*

Patients given DDAVP before urography had higher mean pyelographic scores than those receiving saline (Fig. 3). However, these differences were not statistically significant. The scores in patients given 1 and 4 μg of DDAVP and their matched saline treated controls were higher than for those given 200 ng and their controls. The reason for this difference is unclear as the groups did not differ in age, sex, creatinine clearance or dose of contrast medium given. We presumed it must be due to some seasonal variation.

Since the point of interest was the effect on the X-ray score of a reduction in urine flow by DDAVP, we also examined the pyelographic scores in relation to urine flow rate in individual patients. Figure 4 shows that while in general the highest scores are observed in patients with the lowest urine flows, there is no simple relationship of score to urine flow rate.

Discussion

We have confirmed in man the finding of others in animals (Vavra *et al.*, 1968; Mulder, 1974) that the minimum effective dose of DDAVP in hydrated subjects is 2 ng/kg. However, a dose of this order (200 ng) failed to produce a significant reduction in urine flow rate after contrast medium in fluid restricted patients. Both the fluid restriction, which increases

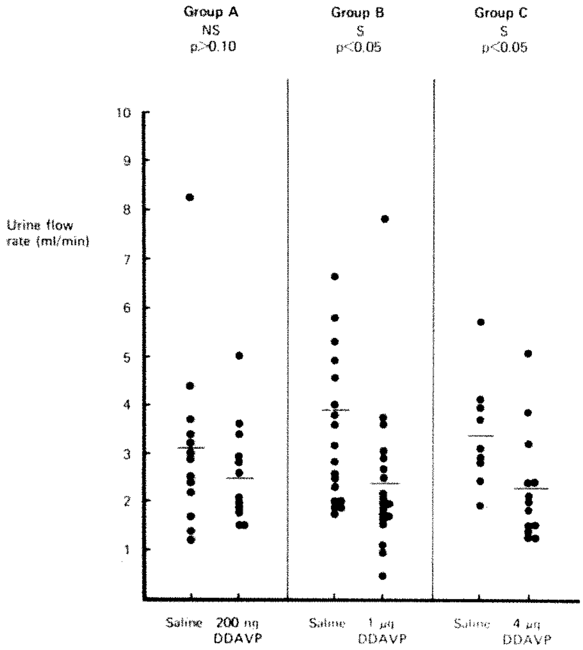


Fig. 2.

The effect of DDAVP on urine flow rate during urography.

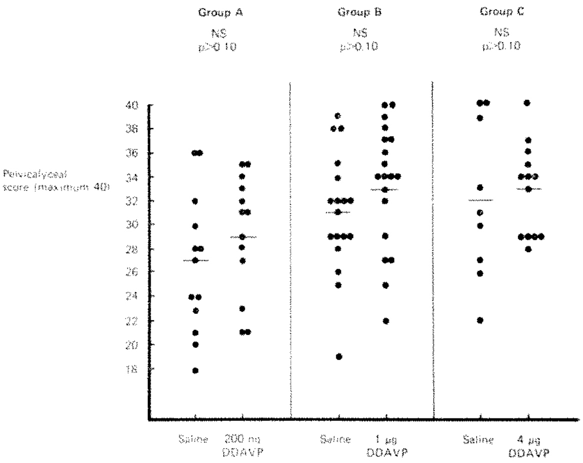


Fig. 3.

The effect of DDAVP on pyelogram quality.

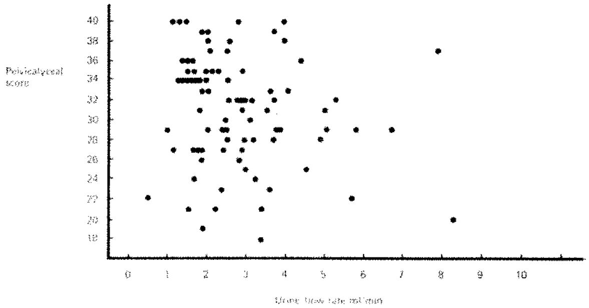


Fig. 4.

Urine flow rate and pelvicalyceal score.

endogenous ADH output, and the osmotic load of the contrast medium probably contributed to this finding. A dose of 1 μg DDAVP, however, did reduce the urine flow significantly despite the osmotic diuresis induced by the contrast medium. No increased effect was observed with 4 μg DDAVP.

Despite this reduction in urine flow rate during urography, we failed to demonstrate a statistically significant improvement in X-ray scores—this despite the fact that any reduction in urine flow rate must be accompanied by a reciprocal increase in urine concentration and so in the concentration of contrast medium. The scatter of pyelogram scores in our patients was considerable (Fig. 3). This is not surprising in view of the multiple factors which affect pyelogram quality and similar scatter has been noted in other studies (Fry *et al.*, 1967; Dacie and Fry, 1971). Allowing for the slightly different scoring techniques, the order of difference in mean score between the saline and DDAVP groups is similar to that observed in hydrated and dehydrated subjects (Fry *et al.*, 1967). With this degree of scatter, a very large number of patients would have to be studied to show any significant difference between the groups.

Given this observation, it is interesting to note (Fig. 4) that there is no simple relationship between urine flow and pyelographic score in this group of patients to whom comparable doses of contrast medium have been given. Thus there is a considerable scatter of scores at low rates of urine flow and some remarkably good scores at much higher rates of urine flow. We must therefore conclude that using this dose of contrast medium in a population with good renal function, the degree of urine concentration is of limited importance.

This may in part be explained by consideration of Fig. 3 where it can be seen that in patients acting as controls in groups given 1 and 4 μg of DDAVP, 16 of 27 patients have scores of 30 or more out of a maximum of 40—*i.e.* there is relatively little room for improvement in these patients, despite their initial urine flow rate of more than 0.6 ml/min.

Our practical conclusion is that in patients with good renal excretory function there appears to be little advantage in the routine administration of DDAVP before intravenous urography. This conclusion does not in any way preclude some possible advantage in administering DDAVP to patients with impaired renal function and especially those with tubular concentrating defects.

ACKNOWLEDGMENTS

We are grateful to Ferring Pharmaceuticals Ltd. who gave financial support for this study. We also wish to thank Miss Peta Baily for her excellent assistance, the Department of Chemical Pathology for osmolality and creatinine analyses, and our colleagues in the X-ray Department who helped us throughout the study.

REFERENCES

ANDERSSON, K. E., ARNER, B., HEDNER, P. and MULDER, J. L. 1972. Effect of 8-lysine-vasopressin and synthetic analogues on release of ACTH. *Acta Endocrinologica, 69*, 640–648.

BENNESS, G. T., 1970. An evaluation of anti-diuretic hormone in intravenous urography ("sniff urography"). *Clinical Radiology, 21*, 157–162.

BREAM, C. A., 1957. The clinical use of pitressin in excretory urography. *American Journal of Roentgenology, 78*, 343–347.

DACIE, J. E. and FRY, I. K., 1971. A comparison of sodium and methylglucamine diatrizoate in clinical urography. *British Journal of Radiology, 44*, 51–54.

EDWARDS, C. R. W., KITAU, M. J., CHARD, T. and BESSER, G. M., 1973. Vasopressin analogue DDAVP in diabetes insipidus: clinical and laboratory studies. *British Medical Journal, 3*, 375–378.

FRY, I. K., CATTELL, W. R., SPENCER, A. G. and PURKISS, P., 1967. The relation between Hypaque excretion and the intravenous urogram. *British Journal of Radiology, 40*, 572–580.

MULDER, J. L., 1974. Personal communication.

VAVRA, I., MACHOVA, A., HOLECEK, V., CORT, J. H., ZAORAL, M. and SORM, F., 1968. Effect of a synthetic analogue of vasopressin in animals and in patients with diabetes insipidus. *Lancet, i*, 948–952.

WALD, M. H. and GALLOWAY, A. F., 1944. Pituitrin for concentrating Diodrast in excretion urography. *Radiology, 43*, 358–363.

WARD, M. K. and FRASER, T. R., 1974. DDAVP in treatment of vasopressin-sensitive diabetes insipidus. *British Medical Journal, iii*, 86–89.

1981, *British Journal of Radiology*, *54*, 488–491

Changes in sizes and distensibility of the aging kidney

By M. McLachlan, M.D. and P. Wasserman

Department of Radiology, University of Rochester Medical Center, Strong Memorial Hospital,
Rochester, New York 14642, USA

(*Received January 1981*)

Abstract

Age-related changes in kidney size and distensibility were examined in 103 patients aged 18 to 89 years without evidence of renal disease or hypertension. Kidney dimensions were measured on radiographs obtained 30 s and 5 min after intravenous injection of contrast agent. Kidney distension was calculated by expressing the difference in area between 30 s and 5 min films as a percentage of the area at 30 s. Distension was not significantly correlated with age but wide variation between individuals may limit the value of measurement of this change in size as a diagnostic test. After middle age, kidney length diminished by approximately 0.5 cm per decade. This reduction implies a loss of kidney weight about double that recorded at necropsy. Post-mortem evidence probably underestimates differences between age groups and age-related diminution in kidney size may be greater than post-mortem evidence suggests.

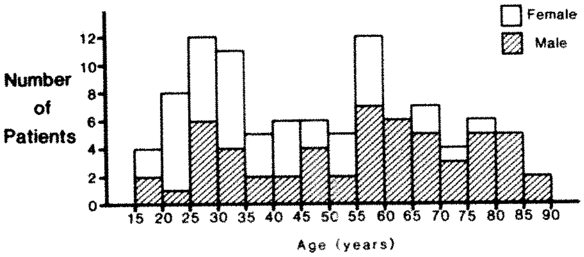


Fig. 1.

Age distribution in males and females in the series.

Few data are available *in vivo* to quantify the loss of renal substance which accompanies aging; information is based almost entirely on necropsy evidence (DeLeon *et al.*, 1933; Wald, 1937). The detailed information readily available for the growing kidney (Hodson *et al.*, 1962; Stolpe *et al.*, 1967) does not exist for the kidney in decline. Moreover, aging is associated with changes in the renal vessels, the nephron and the interstitium (McLachlan, 1978), which might be expected to reduce the capacity of the kidney to distend after intravenous contrast agent (Swann, 1960). This possibility has received little attention though changes in distensibility have been used in the diagnosis of renovascular hypertension (Dorph and Oigaard, 1973b).

We have measured kidney size and distensibility on the intravenous urograms of more than 100 adults without evidence of hypertension or renal disease. We have related these measurements to the patients' age.

Materials and Methods

One hundred and three patients, examined by intravenous urography at Strong Memorial Hospital over a period of eight months, were selected for study. Fifty-six were male aged 18–89 years (mean 59; SD 19.5 years); 47 were female aged 17–79 years (mean 39; SD 16.0 years) (Fig. 1). The difference in age is significant ($P < 0.001$) and results from exclusion of many women in older age groups because of hypertension or diabetes (see below). Eighty-three were white, 20 black. Medical records of all patients were examined. Patients with known or suspected renal disease, on the basis of clinical, biochemical or radiological evidence, were excluded. A history of diabetes mellitus, glycosuria, hypertension, sickle cell disease or trait, or urinary tract calculi also constituted grounds for exclusion.

Patients were prepared for intravenous urography by purgation and overnight deprivation of fluids. Their blood pressure was recorded by sphygmomanometer immediately before intravenous urography. Those with a diastolic pressure greater than 100 mmHg at that time were excluded. Mean diastolic pressure was 72 (SD 9.5) mmHg with no significant differences between white and black patients or between males and females. Patients received 1.5 ml per kg body weight Renografin 60 (sodium and meglumine diatrizoate; Squibb) injected intravenously by hand in 30 to 60 s. Radiographs of the renal areas were obtained in expiration without abdominal compression 30 s and 5 min after the end of injection. Focus–film distance was 100 cm; table top to film distance was 5 cm. Renal outlines were traced on 30 s and 5 min films and renal areas measured by using a digitizing tablet interfaced to a mini-computer system which recorded the co-ordinates of the points of which the traced contours were composed. The computer calculated renal areas from the contour co-ordinates and a scale factor entered by the operator. When, on the 5 min film, the hilum was obscured by an opaque pelvis, the hilar contour demonstrated on the 30 s film was followed. Kidney length was measured only on the

30 s film. Two right and 14 left kidneys could not be measured. Measurements from another patient, with a unilateral duplex system, were used only to assess renal distensibility. Renal distension after injection of contrast agent was calculated as $(A_5 - A_{\frac{1}{2}})/A_{\frac{1}{2}} \times 100$, where A_5 is renal area at 5 min and $A_{\frac{1}{2}}$ is area at 30 s. All measurements were made by the same observer (P.W.). The data were analysed by linear regression analysis or by Student's *t*-test for paired or unpaired observations as appropriate. Probability values of less than 0.05 were considered to be significant, and were based on numbers of patients, not numbers of kidneys.

RESULTS

Figure 2 shows kidney length (A) and area (B) by age group. Patients older than 75 years had significantly smaller kidneys than middle-aged patients. For patients aged 50 and over a significant negative correlation existed between age and kidney length ($n=49$; $r=-0.41$; $p<0.01$) and area ($n=49$; $r=-0.42$; $p<0.01$). Because the younger age groups contained more women than men, their mean values tended to be lower. No significant differences in kidney dimensions existed between white and black patients. Mean length and area on the left were 13.56 (SD 1.30) cm and 73.51 (SD 12.63) cm^2. On the right they were 13.23 (SD 1.22) cm and 69·66 (SD 11.30) cm^2. The differences are significant ($p<0.001$).

Figure 3 relates age and renal distension after contrast agent. There was no significant correlation. Renal distension was not significantly correlated with blood pressure. Multiple regression analysis also showed no significant correlation between distension, age and blood pressure. Mean increase in renal area was 2.5 (SD 3.3)%; it ranged from 14.0 to −5.8%. There were no significant differences between males and females or between white and black patients.

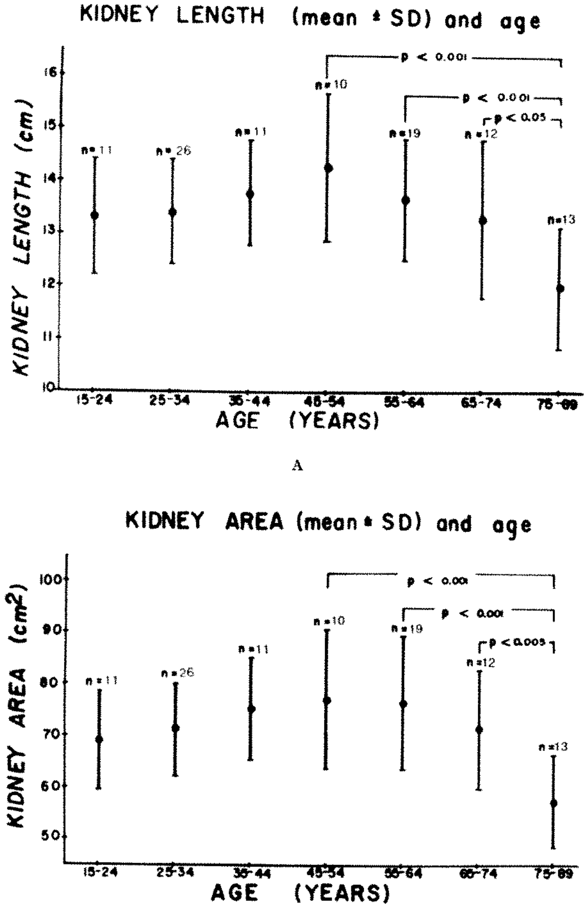


FIG. 2.

Kidney length (A) and area (B) are grouped according to age. The decline in dimensions after the middle years is greater than expected from necropsy evidence (see text). The preponderance of women in the younger age groups accounts for the slightly smaller kidneys in these groups. Numbers of patients in each group and significant differences between groups are indicated above the bars.

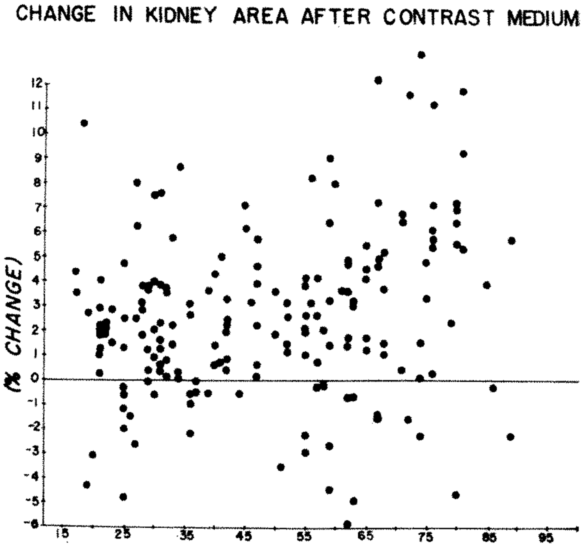


FIG. 3.

This relates the percentage change in kidney area following contrast medium to age. There is no significant correlation. Mean increase in area was 2.5%, with wide variation between individuals.

Discussion

Distension of the kidney after intravenous contrast agent has been ascribed to vascular and tubular dilatation and to an increase in interstitial pressure (Dorph and Oigaard, 1973a; Dorph *et al.*, 1977; Hegedus *et al.*, 1978). Increase in renal area, maximal 5 min after injection, is usually about 5% in normotensive individuals (Dorph and Oigaard, 1973a) and appears not to be dose-related (Wolpert, 1965; Dorph and Oigaard, 1973a; Dorph *et al.*, 1977). We noted a smaller mean increase, but variation between individuals was wide. Swann (1960), who studied in detail this "functional distension" of the kidney, predicted a reduction in distensibility with aging. This is a reasonable conclusion. Not only is there a well-established relationship between aging and sclerosis of arteries and arterioles (Bell, 1950; Oliver, 1952; Darmady *et al.*, 1973) but the capacity of these vessels to dilate in response to acetylcholine or sodium loading also diminishes with age (Hollenberg *et al.*, 1974). As an accompaniment to these events, nephrons decline in number and the proportion of sclerotic glomeruli rises among those that remain (Moore, 1931; Kaplan *et al.*, 1975; McLachlan *et al.*, 1977). The amount of interstitial fibrosis, particularly in the medulla, also increases (Keresztury and Megyeri, 1962; Darmady *et al.*, 1973). Despite these changes, we found no age-related alteration in the capacity of the kidney to distend. The value of measuring this change in size for the purpose of diagnosis (Dorph and Oigaard, 1973b) does not appear to depend on the age of the patient. However, wide variation between individuals, which Dorph and Oigaard (1973a; b) also observed, may limit its usefulness.

Necropsy evidence suggests that the weight of the adult human kidney remains constant until the fifth decade of life; between then and the eighth decade its weight diminishes by about 20% (DeLeon *et al.*, 1933; Wald, 1937). The decline in kidney dimensions visible at intravenous urography is less completely documented. Hodson (1960) stated only that there is usually a "slow decrease in the size of the kidneys which progresses to the small senile kidneys of old age". Simon (1964), who measured renal length on plain films, recorded a reduction of 0.8 cm (about 7%) between the fifth and ninth decades. Post-mortem kidney weight in these subjects diminished by 26%. On this evidence, he concluded that length provided a poor indicator of the decline in weight because replacement of tissue by renal sinus fat occurred without significant change in external dimensions. However, if these linear dimensions are raised to the same mathematical dimension as weight, *i.e.* if renal length is cubed, the 7% reduction in length implies a loss of weight of about 20%. Griffiths *et al.* (1974) noted only a slight increase in renal sinus fat with age and demonstrated a highly significant correlation between post-mortem kidney weight and length. In the present study, the kidneys of patients aged 75 and over, most of whom were men, were more than 2 cm shorter than those of middle-aged patients, a difference greater than 15%. In three-dimensional terms this represents a loss of about 40%. Calculations based on area give similar results. If only men are considered, the decrease is slightly greater because the preponderance of women in the younger age groups tends to lower mean dimensions in these groups.

This loss of substance is double that recorded at necropsy (DeLeon *et al.*, 1933; Wald, 1937). We consider our measurements to be accurate. Renal length is readily measured, especially during the nephrogram phase, though we recognize difficulties (Cardiff–Oxford Bacteriuria Study Group, 1979). To avoid many of these, films were obtained in expiration, without abdominal compression, after a weight-related dose of contrast agent; one of us (P.W.) measured all kidneys. Kidney weight at necropsy, even after sudden, accidental death (DeLeon *et al.*, 1933; Wald, 1937) must differ from kidney weight *in vivo*. Renal volume may decrease by up to 40% as a result of a fall in systemic blood pressure (Hodson, 1961; Collier and Swann, 1971) and kidneys are known to diminish markedly in size after death (Moell, 1961). Because renal blood flow declines by about 1% per year after the second or third decade (Wesson, 1969; Hollenberg *et al.*, 1974), the reduction in kidney size when blood flow ceases at death is likely to be less in the elderly than it is in younger subjects. Our results suggest that the age-related reduction in renal volume may be much greater than post-mortem information (DeLeon *et al.*, 1933; Wald, 1937) indicates. We are reinforced in this belief by measurements obtained by computerized tomography in another group of patients since the present study was completed (McLachlan and Kaplan, unpublished). These results also imply a reduction in kidney volume in the elderly approximately twice that recorded at necropsy (DeLeon *et al.*, 1933; Wald, 1937).

Acknowledgments

We thank Robert C. Waag, Ph.D. for his help. Mary Jo McMannis, R.T., Barbara S. Paris, R.T. and Gary M. Martin, R.T. performed the intravenous urograms. We acknowledge the support of the Department of Radiology in the form of a Summer Fellowship awarded to one of us (P.W.).

REFERENCES

Bell, E. T. 1950. *Renal Disease*, 2nd ed. (Lea and Febiger, Philadelphia), pp. 331–346.

Cardiff-Oxford Bacteriuria Study Group, 1979. Long-term effects of bacteriuria on the urinary tract in schoolgirls. *Radiology, 132,* 343–350.

Collier, R. O. and Swann, H. G., 1971. Relation of kidney size to blood pressure. *American Journal of Physiology, 12,* 91–94.

Darmady, E. M., Offer, J. and Woodhouse, M. A., 1973. The parameters of the ageing kidney. *Journal of Pathology, 109,* 195–207.

DeLeon, W., Garcia, A. and DeJesus, P. I., 1933. Normal weights of visceral organs in adult Filipinos. *Philippine Journal of Science, 52,* 111–127.

Dorph, S. and Oigaard, A., 1973a. Variations in renal size of the normal kidney following intravenous administration of water-soluble contrast medium and urea. *British Journal of Radiology, 46,* 183–186.

1973b. Variations in renal size in the diagnosis of renovascular hypertension. *British Journal of Radiology, 46,* 187–190.

Dorph, S., Sovak, M., Talner, L. B. and Rosen, L., 1977. Why does kidney size change during I.V. urography? *Investigative Radiology, 12,* 246–250.

Griffiths, G. J., Cartwright, C. and McLachlan, M. S. F., 1974. Estimation of renal size from radiographs: is the effort worthwhile? *Clinical Radiology, 26,* 249–256.

Hegedus, V., Faarup, P., Norgaard, T. and Lonholdt, C., 1978. Volume changes in the rat renal cortex during urography. *British Journal of Radiology, 51,* 793–798.

Hodson, C. J., 1960. Hypertension of renal origin. In *Modern Trends in Diagnostic Radiology*, Ed. J. W. McLaren (Hoeber, Inc., New York), pp. 124–134.

1961. Physiological changes in size of the human kidney. *Clinical Radiology, 12,* 91–94.

Hodson, C. J., Drewe, J. A., Karn, M. N. and King, A., 1962. Renal size in normal children: a radiographic study during life. *Archives of Disease in Childhood, 37,* 616–622.

Hollenberg, N. K., Adams, D. F., Solomon, H. S., Rashid, A., Abrams, H. L. and Merrill, J. P., 1974. Senescence and the renal vasculature in normal man. *Circulation Research, 34,* 309–316.

Kaplan, C., Pasternack, B., Shah, H. and Gallo, G., 1975. Age-related incidence of sclerotic glomeruli in human kidneys. *American Journal of Pathology, 80,* 227–234.

Kereszturry, S. and Megyeri, L., 1962. Histology of renal pyramids with special regard to changes due to ageing. *Acta Morphologica Academiae Scientiarum Hungaricae, 11,* 205–215.

McLachlan, M. S. F., 1978. The ageing kidney. *Lancet, ii,* 143–146.

McLachlan, M. S. F., Guthrie, J. C., Anderson, C. K. and Fulker, M. J., 1977. Vascular and glomerular changes in the ageing kidney. *Journal of Pathology, 121,* 65–78.

Moell, H., 1961. Kidney size and its deviation from normal in acute renal failure. *Acta Radiologica: Diagnosis Supplement, 206,* 1–74.

Moore, R. A., 1931. The total number of glomeruli in the normal human kidney. *Anatomical Record, 48,* 153–168.

Oliver, J., 1952. Urinary system. In *Cowdry's Problems of Aging.* Ed. A. I. Lansing (Williams and Wilkins, Baltimore), pp. 631–650.

Simon, A. L., 1964. Norman renal size: an absolute criterion. *American Journal of Roentgenology, 92,* 270–272.

Stolpe, Y., King, L. R. and White, H., 1967. The normal range of renal size in children. *Investigative Urology, 4,* 600–607.

Swann, H. G., 1960. The functional distension of the kidney: a review. *Texas Reports on Biology and Medicine, 18,* 566.

Wald, H., 1937. The weight of normal adult human kidneys and its variability. *Archives of Pathology, 23,* 493–500.

Wesson, L. G., 1969. Renal hemodynamics in physiological stress. In *Physiology of the Human Kidney* (Grune and Stratton, New York), pp. 96–108.

Wolpert, S. M., 1965. Variation in kidney length during the intravenous pyelogram. *British Journal of Radiology, 38,* 100–103.

Book review

Trattato di Senologia. By L. Oliva and P. de Albertis, pp. ix+399, 1980 (Piccin, Padua), L. 90,000.
ISBN 88-212-0787-0

The original publication by the main authors of this work was a treatise on mammography. This was apparently well received. When requested to produce another edition they decided to improve and expand the work as the existing Italian literature required a more comprehensive "Treatise on examination of the breast". This volume is the result. Experts in the various diagnostic modalities useful in investigation of breast disease were invited to collaborate on the production of this new book.

The whole field of diagnostic techniques has been covered. Clinical examination, mammography, xeromammography, galactography, pneumocystography, arteriography, diaphonoscopy, thermography, echography and cytology are included. The physical bases of the various imaging techniques are also discussed. The account and illustrations of echography are particularly good and instructive.

The publisher has been kind, on the whole, in the quality of reproduction of the mammograms. Some have obviously suffered. Most of the xerograms are technically underexposed and over-developed, but show the described features.

There are a few points that the reviewer cannot accept without comment. One of the mammographic signs of malignancy is stated to be "peritumoral oedema" on pages 86 and 87. This "oedema" is divided into "opaque oedema" and "radio-transparent oedema". In the reviewer's opinion this radio-transparent area is due to distorted fat and not oedema. It is the radiological demonstration of the well-known clinical sign of "pseudo-lipoma" associated with carcinoma. Unfortunately on page 116, Fig. 3–104, the authors use the term "pseudo-lipoma" for the normal appearance of breast fat interspersed in glandular tissue. This may look like a lipoma, but is normal fat tissue. It is a pseudo-lipoma in that it is not a true lipoma but the term "pseudo-lipoma" should be restricted to the sign associated with breast carcinoma.

The only drawback of this treatise is that it is written in Italian.

I. H. Gravelle.

1981, *British Journal of Radiology*, *54*, 492–495

Severe complications from partial splenic embolization in patients with liver failure

By I. Vujic, M.D. and J. W. Lauver, M.D.

Department of Radiology, Medical University of South Carolina, Charleston, SC 29403, USA

(*Received October 1980 and in revised form January 1981*)

ABSTRACT

Transcatheter embolization of the spleen is gaining popularity as a non-surgical method of treatment for hypersplenism. While early reports documented frequent serious complications, a more recent study noted good results using a fractionated approach with only partial embolization of the periphery of the spleen. This technique was recently used on three patients with hypersplenism associated with severe liver disease. All had grave complications, including sepsis, pneumonia, abscess formation, and progressive liver failure, and all died within six weeks of the angiographic procedure in spite of good haematological responses. Since it is frequently this category of patient in whom the procedure is attempted, definitive surgical splenectomy is suggested following the embolization as soon as the clotting parameters return to normal.

Non-surgical splenectomy via embolization of the splenic artery was first attempted in 1973 by Maddison. Since that time multiple attempts to evaluate the benefits and risks of this procedure have been made, mostly as experimental work on dogs (Chuang and Reuter, 1975a; Anderson *et al.*, 1977) and occasionally on humans who were at high risk for a surgical procedure.

Our experience in the last two years has included three patients suffering from hypersplenism. Embolization was achieved by combined injection of small particles of Gelfoam and a small amount of Gelfoam powder, the latter injected near the end of the procedure. These small particles and powder were used to obliterate only a portion of the peripheral splenic bed. Forward flow through the splenic circulation was deliberately preserved and the splenic vein was subsequently visualized in two of our patients. Two patients died within ten days of embolization and one patient survived the procedure for six weeks. Their courses are described.

CASE REPORTS

Case 1

A 33-year-old white male was being evaluated for hepatic failure secondary to jejuno-ileal bypass which produced a short bowel syndrome. The patient had portal hypertension with massive splenomegaly and hypersplenism resulting in marked depression of circulating platelets and leucocytes secondary to sequestration. Since the patient's condition contraindicated surgery, arteriography with partial embolization of the spleen was considered an alternative which could improve his clotting parameters. An immediate favourable response to embolization was achieved with the platelet count rising from 20 000 immediately prior to embolization to 150 000 on the fourth day after embolization. Nonetheless, liver function rapidly deteriorated with lethargy progressing to coma and death. The cause of death was considered to be a pulmonary embolus on the sixth day post embolization. No autopsy was obtained.

Case 2

A 54-year-old white male was hospitalized for bleeding from an umbilical varix. There was a long history of ethanol abuse with hospitalizations for portal hypertension, hepatosplenomegaly and ascites. His last hospital admission was complicated by recurrent bleeding from the umbilical varix and hypersplenism with a persistently low platelet count for which transcatheter embolization of the spleen was performed. The splenic vascular bed was only partially embolized (Fig. 1A). Following the procedure, the platelet

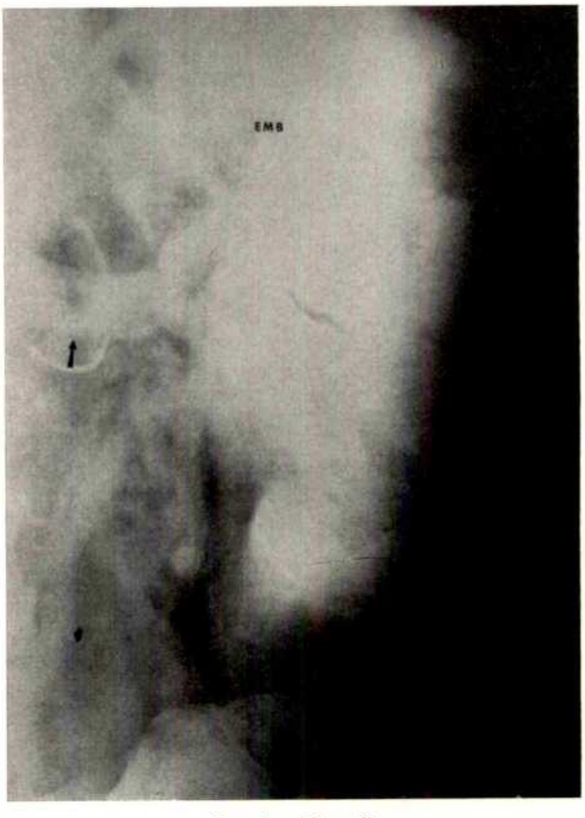


FIG. 1A. (*Case 2*).

Arteriogram after embolization demonstrates hepatopedal flow in splenic vein (arrows) and some hepatofugal flow through collaterals (arrowheads). Note obliteration of peripheral vascular bed with preservation of flow through spleen.

Address for reprints: Ivan Vujic, M.D., Department of Radiology, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29403, USA.

count rose steadily after an initial drop. A normal value of 252000 was reached on the sixth day post splenectomy following a low of 36 500 on the second day. The patient soon developed electrolyte imbalances, bacterial peritonitis and septic shock, which precipitated progressive renal failure despite extensive antibiotic coverage. The patient's course worsened with increasing lethargy and end-stage hepatorenal syndrome. He expired five-and-a-half weeks following the embolization. At autopsy multiple large abscesses were present in the periphery of the spleen. Post-mortem splenic angiogram revealed persistent occlusion of the peripheral vascular bed (Fig. 1B).

Case 3

A 15-year-old white female was hospitalized for evaluation of splenomegaly. The patient had been diagnosed as having cystic fibrosis at the age of three and had done fairly well between occasional episodes of pneumonia and haemoptysis. The splenomegaly was associated with hypersplenism. During the hospitalization the patient developed marked haematemesis requiring multiple transfusions and was further found to have cirrhosis and oesophageal varices, Progressive respiratory difficulties required intubation. The platelet count dropped to 35 000 and did not improve significantly despite platelet transfusions. Because of continued bleeding and thrombocytopenia, the patient underwent angiography with embolization of the splenic artery in an attempt to influence the haemorrhagic diathesis by controlling the hypersplenism. Following the procedure the platelet count rose to 152 000 on the fourth day post embolization and stabilized near this level. Transhepatic portography and sclerosis of the coronary vein were also undertaken to arrest the bleeding oesophageal varices. However, the patient later bled from other sites and had a progressive downhill course complicated by pneumonia, pneumothorax and staphylococcal septicaemia. She died on the ninth day post embolization. Autopsy showed an infarcted and necrotic spleen, although no evidence of abscess formation was seen grossly. Injection of the splenic circulation with a radiopaque contrast agent revealed multiple small necrotic cavities assumed to be secondary to infarction with liquefaction necrosis (Fig. 2).

DISCUSSION

Ablation of the spleen by intentional infarction should be beneficial in those patients who require splenectomy but are poor candidates for surgery. Patients suffering from certain blood dyscrasias and extensive thrombocytolysis as seen in hypersplenism

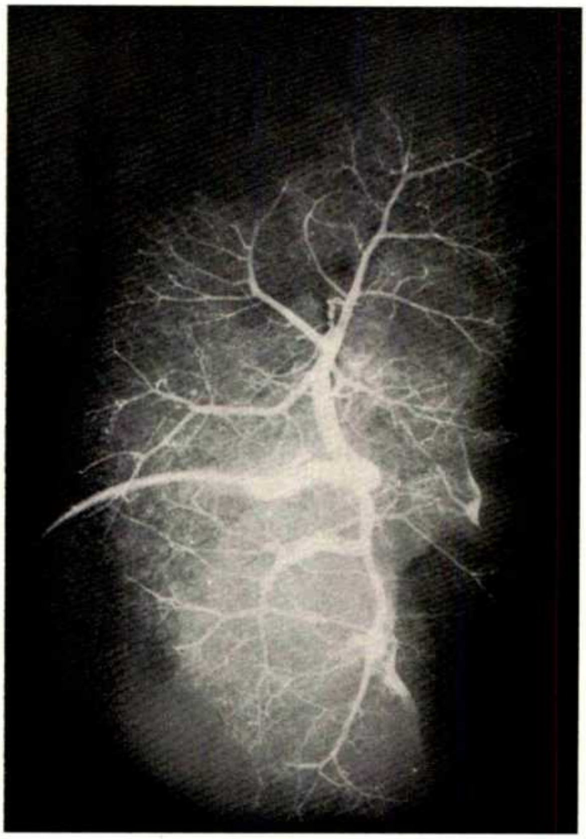


FIG. 1B. (*Case 2*).

Post mortem splenic arteriogram demonstrates occlusion of portions of peripheral splenic vascular bed. Cut sections revealed large peripheral abscesses throughout the spleen.

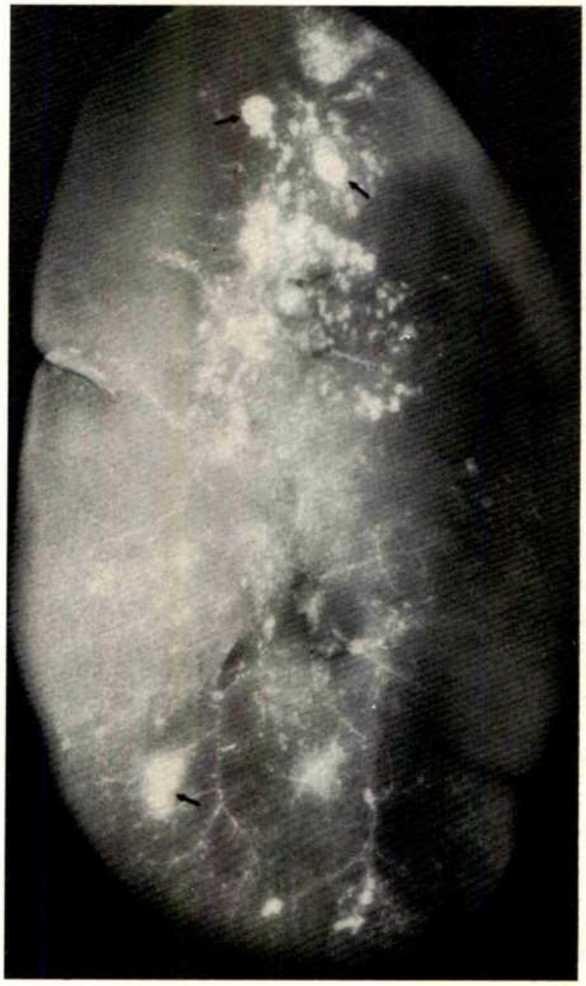


FIG. 2. (*Case 3*).

Post-mortem angiogram with barium reveals multiple small necrotic cavities from infarction. Note avascular periphery.

are the major group of patients who could benefit from this procedure. Also, severe variceal bleeding in portal hypertension can be temporarily controlled in some patients by obliteration of the splenic circulation (Bucheler *et al.*, 1975). This can eliminate the need for an emergency portosystemic shunt and defer it for an elective procedure with a lower mortality. Post-traumatic splenic bleeding has been controlled by embolization (Chuang and Reuter, 1975b; Guilford and Scatliff, 1976) and although the procedure has not replaced surgical splenectomy, it may be considered for severely injured patients who might not survive surgical exploration. The well-established fact that splenectomized patients, particularly children, are very susceptible to infection would further encourage the need for non-surgical attempts to selectively control sites of bleeding from splenic trauma (Erickson *et al.*, 1968).

Controversy arises regarding the method by which embolization of the splenic circulation should be accomplished. There is adequate evidence to support that simple occlusion of the proximal splenic artery does not trigger a significant haematological response (Anderson *et al.*, 1977). The failure to respond is attributed to the abundant collateral circulation through the gastric and gastro-epiploic arteries which re-establish the blood supply to the spleen around the occluded segment of splenic artery. As a consequence, no significant alteration of splenic morphology occurs. Peripheral occlusions achieved by Gelfoam powder and small particles are responsible for significant morphological and haematological changes (Anderson *et al.*, 1977; Castaneda-Zuniga *et al.*, 1977) but unfortunately this method is associated with a high incidence of complications. Massive splenic infarction and abscess formation as well as splenic vein thrombosis have been previously documented (Anderson *et al.*, 1977; Castaneda-Zuniga *et al.*, 1977; Lunderquist, 1978). Massive infarction is particularly evident with the "one stage" procedure (Castaneda-Zuniga *et al.*, 1977; Wholey *et al.*, 1978) but this can be avoided by fractionating the procedure into two or three stages.

Abscess formation is the most dangerous complication. The aetiology is complex, but the present hypothesis is that a decrease in the immunological response of the patient, splenic hypoxia which brings about the proliferation of anaerobic bacteria, introduction of bacteria with the catheter and contamination of the ischaemic splenic bed with intestinal organisms produced by retrograde flow in the splenic vein are the most significant factors responsible for the suppurative complications (Anderson *et al.*, 1977; Wholey *et al.*, 1978; Spigos *et al.*, 1979).

A recent report of 13 successful transcatheter splenectomies using small particles of Gelfoam without complication is contrary to most reported series (Spigos *et al.*, 1979). Our procedures were carried out with the same technique, except that Betadine baths were omitted. The fact that all three of our patients were in a terminal stage of liver disease undoubtedly contributed to the poor results. The post-mortem angiograms in the one case revealed cavities suggestive of early abscess formation, and in the patient who survived for a longer period multiple peripheral splenic abscesses were encountered at autopsy. These complications were previously observed by other investigators. Particularly impressive was the follow-up in our Case 2. Less than half of the peripheral splenic vascular bed was ablated and a very favourable haematological response was accomplished on the sixth and seventh post procedural days, but the patient subsequently developed septicaemia and peritonitis on the tenth day despite extensive antibiotic coverage. At the time of death multiple large peripheral abscesses were evident in the spleen. An additional striking feature in our follow-up period was distinct differences in the ways the patients tolerated non-surgical splenectomy. The responses in our three patients were variable and not entirely related to the magnitude of occlusion achieved.

Despite the modified two or three stage technique, splenic abscess is still a complication of the "medical" splenectomy. Therefore, definitive surgical splenectomy is suggested following the embolization as soon as the platelet count approaches normal values as has been suggested by other investigators (Castaneda-Zuniga *et al.*, 1977).

It is conceivable that a multiple-stage non-surgical splenectomy may in the near future replace surgical splenectomy in patients not severely compromised. Only a small fraction of the splenic vascular bed should be embolized at each stage, allowing time for recovery between stages. This less aggressive approach which entails multiple procedures could create a sequence of events similar to that which takes place in the spleens of patients with sickle-cell disease.

REFERENCES

Anderson, J. H., VuBan, A., Wallace, S., Hester, J. P. and Burke, J. S., 1977. Transcatheter splenic arterial occlusion: An experimental study in dogs. *Radiology*, *125*, 95–102.

Bucheler, E., Thelen, M., Schirmer, G., Schultz, D., Frommhold, H., Siedeck, M. and Kaufer, C., 1975. Catheter embolization of the splenic artery as treatment for acute bleeding from varices. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin*, *122*, 224–229.

CASTANEDA-ZUNIGA, W. R., HAMMERSCHMIDT, D. E., SANCHEZ, R. and AMPLATZ, K., 1977. Nonsurgical splenectomy. *American Journal of Roentgenology, 129,* 805–811.

CHUANG, V. P. and REUTER, S. R., 1975a. Experimental diminution of splenic function by selective embolization of the splenic artery. *Surgery Gynecology and Obstetrics, 140,* 715–720.

1975b. Selective arterial embolization for the control of traumatic splenic bleeding. *Investigative Radiology, 10,* 18–24.

ERICKSON, W. D., BURGERT, E. O. and LYNN, H. B., 1968. The hazard of infection following splenectomy in children. *American Journal of Diseases in Children, 116,* 1–12.

GUILFORD, W. B. and SCATLIFF, J. H., 1976. Transcatheter embolization of the spleen for control of splenic haemorrhage and *in situ* splenectomy: an experimental study using silicone spheres. *Radiology, 119,* 549–553.

LUNDERQUIST, A., 1978. Interventional Radiology Meeting, Boston, October.

MADDISON, F. E., 1973. Embolic therapy of hypersplenism. *Investigative Radiology, 8,* 280–281.

SPIGOS, D. G., JONASSON, O., MOZES, M. and CAPEK, V., 1979. Partial splenic embolization in the treatment of hypersplenism. *American Journal of Roentgenology, 132,* 777—782.

WHOLEY, M. H., CHAMORRO, H. A., RAO, G. and CHAPMAN, W., 1978. Splenic infarction and spontaneous rupture of the spleen after therapeutic embolization. *Cardiovascular Radiology, 1,* 249–253.

Book review

Forensic Fetal Osteology. By I. Gy. Fazekas and F. Kósa. Translated by E. Kerner. pp. 414, 62 figs., 207 tables, 1978 (Akadémiai Kiadó, Budapest), $36.00.
ISBN 963–05–1491–5

Part of the forensic pathologist's task is to examine an often incomplete collection of bones and give the sex and the age of the person from which they came. For adult bones there are well-tried methods but until recently the information on fetal bones has been scanty and this book sets out to correct the omission. An enormous collection of facts and figures has been built up by the authors during 20 years of practice in forensic medicine and this provides the data from which it is possible to predict fetal length and age with remarkable accuracy from any one of a large number of fetal bones.

The data upon which the book is based are from 138 human fetuses (17 males and 67 females) ranging in age from the third to the tenth lunar month. The first few chapters describe the principles and methods employed during the examination and measurement of fetal bones. Exact descriptions, accompanied by annoted photographs, are given for the dimensions of the bones including those of the skull, ribs, limb girdles and long bones, as well as those of the vertebral column, the extremities and the auditory ossicles. There is a full discussion of the statistical methods used although these are of the standard variety. The graphs give bone length regressed on body length and standard age for body length markers are superimposed on these. A standard series of female and male fetal skeletons aged at half-monthly intervals is photographed with the dimensions of each bone given alongside.

The middle and largest section of the book is devoted to the individual bones of the skeleton. The raw data of all the dimensions are given together with the mean values and these figures are set out in numerous tables, graphs and regression diagrams for each bone at half-monthly intervals. The present findings are compared with previous work. The last section of the book deals with miscellaneous subjects of interest to the forensic pathologist including distinguishing human from animal remains, blood-group testing on bones and changes in size of bones caused by heat. There is an extensive bibliography containing many German, Polish and Hungarian references.

It is assumed that the book has suffered somewhat in translation from the Hungarian as there are occasional clumsy constructions. Some parts, for example the description of the developing vertebrae, are very heavy going; occasionally old fashioned terms, such as epistropheus for axis are used, which have not been normal anatomical nomenclature since 1955. The results obtained from the measurement of the auditory ossicles are of doubtful practical use. Because of a not surprisingly poorer correlation between the size and body length, the authors state that it is important that these bones are measured with a precision of 0.1 mm. It is debatable if this is a repeatable observation or if this degree of exactitude has any real biological significance.

Despite these comparatively minor considerations, the book contains a wealth of observations, facts and figures. It will be of use to the practising forensic pathologist and also provide useful reference material for anatomists, embryologists and obstetricians.

J. L. SCHEUER.

Ultrasound of the Pediatric Abdomen and Pelvis. A Correlative Imaging Approach. By Hooshang Kangarloo and W. Fred Sample, pp. xvi+375, 1980 (YB Medical Publishers, Chicago/London), £33·73.
ISBN 0–8151–4972–7

This book by American authors summarizes the use not only of ultrasound but also of other imaging techniques, including conventional radiology and CT, in the investigation of paediatric abdominal and pelvic pathology. The quality of the images is very satisfactory and the authors' discussions on the roles of the different imaging techniques in particular clinical situations is especially valuable. In addition the relevant embryology and intra-uterine ultrasound findings in certain conditions are also discussed and illustrated and this is a refreshing new approach which I found most helpful.

The name of the first author was previously unknown to me though the work of the late Fred Sample is both well known and well respected by most ultrasonographers. The quality of this book compares well with the high standards set in all Dr. Sample's previous publications and it can therefore be highly recommended to both paediatricians and paediatric radiologists, as well as all ultrasonographers and ultrasonologists who have from time to time to examine paediatric cases.

H. B. MEIRE.

1981, *British Journal of Radiology*, 54, 496–499

The herniographic appearance of direct inguinal hernias in adults

By O. Ekberg, M.D.

Department of Diagnostic Radiology, Malmö General Hospital, S-214 01 Malmö, Sweden

(*Received August 1980*)

ABSTRACT

Inguinal hernias can be demonstrated by positive contrast herniography in children and adults. In this latter age-group direct inguinal hernias are frequent and can appear with different location and shape. In this series of 39 inguinal hernias in 25 adults five different types could be distinguished, according to location. Lateral direct inguinal hernias were found protruding in an anterior direction from the medial inguinal fossa. Inguinofemoral hernias protruded in a mainly inferior direction from the medial inguinal fossa. Medial direct inguinal hernias protruded from the lateral region of the supravesical fossa just medial to the medial inguinal fold. Diverticular direct inguinal hernias were located in the medial aspect of the supravesical fossa. Supravesical inguinal hernias were located in the mid-line. The distinction between these direct hernias and their relation to and distinction from other hernias in the inguinal region is discussed.

Positive contrast herniography has long been used to demonstrate inguinal hernias in a paediatric age-group (Ducharme *et al.*, 1967; White *et al.*, 1968; Shackelford and McAlister, 1972; Oh *et al.*, 1978). Gullmo (1973; 1980) has adopted a similar technique for adult patients with unclear groin pain. Among groin hernias the indirect, femoral and obturator hernias have a fairly constant appearance on the herniogram. This is in contrast to the direct hernias which can exhibit a variable appearance according to their location and shape. The aim of this study is to describe the herniographic appearance of five different types of direct inguinal hernia. Their differentiation from other types of groin hernias is discussed.

Included in this report are those inguinal hernias which protrude medial to the lateral umbilical fold (inferior epigastric vessels) from the medial inguinal fossa and supravesical fossa.

MATERIAL

During 1977 and 1978 a total of 39 direct inguinal hernias were demonstrated in 25 patients (16 men and nine women). The age of the patients varied between 18 and 78 years with a mean age of 45 years. The symptoms of the patients were vague and related to pain in one or both groins which could indicate the presence of a hernia. However, in all 25 patients the physical examination was within normal limits. In no patient could any hernia be palpated. There were nine patients who had been operated upon because of an inguinal hernia earlier.

EXAMINATION TECHNIQUE

Puncture of the abdominal cavity was made with a 10 cm long needle with an outer diameter of 0·9 mm. As a contrast medium we used 80 ml of meglumine metrizoate with an iodine content of 200 mg/ml. Following the injection the patient was placed prone with the head of the table elevated 20°. The patient was asked to roll from side to side for five minutes, which caused the contrast medium to be evenly distributed in the groin area. With the patient straining, PA views of the groin area were then obtained with and without the tube angled 25° caudally. Films with the patient in the RPO and LPO were also obtained.

RESULTS

Among the 39 direct hernias in this series, 26 were found on the right and 11 on the left side, while two were in the mid-line. Hernias on both the right and left sides were found in eight patients. Both direct and indirect inguinal hernias were found in nine patients. There was both a direct and a femoral hernia in one patient. Extremely deep inguinal fossae and/or pouch of Douglas were found in 16 patients.

According to the location and shape of the direct hernias five different types were identified on the herniograms, namely: lateral, inguinofemoral, medial, diverticular and supravesical direct inguinal hernias.

Lateral direct inguinal hernias

There were 23 of this type, and 15 were found in men. They protruded from the medial inguinal fossa between the medial and lateral umbilical folds and extended in anterior and superior direction in relation to the abdominal wall and inguinal ligament (Poupart's). These hernias were hemispherical, with a fairly broad base and they had no distinct neck, although there was sometimes a slight notch at the base due to the medial and lateral umbilical folds. One hernia had an attendant accessory loculus which arose from its lateral border (Fig. 1). The hernias varied in size between 2×2 cm and 7×4 cm (width×length). In 17 of the hernias there was a loop of bowel or omentum.

Inguinofemoral hernias

There were five such hernias, three in women. They protruded in an inferior and anterior direction from the inferior aspect of the medial inguinal fossa (Fig. 2). They protruded at right angles to the inguinal ligament and had a typical triangular shape with a slight convex lateral border which made the apex of the fundus of the hernia point in an inferior–medial direction. Due to their location these hernias were best seen on straight frontal views obtained without angling of the tube. There were three hernias which contained bowel.

Medial direct inguinal hernias

There were seven of this type, four in women. These hernias protruded from the lateral region of the supravesical fossa medial to the medial umbilical fold. They were square and protruded at right angles to the abdominal wall (Fig. 3). Their size varied between 3×3 cm and 3×5 cm. Five of these hernias contained bowel.

Diverticular direct inguinal hernias

One man who had had four operations for hernia, and one non-operated man, exhibited this type of hernia. The hernias were located in the medial aspect of the supravesical fossa. They had distinct necks and extended anteriorly (Fig. 4); one contained a loop of bowel. The sizes of the hernias were 2×5 cm and 3×4 cm, respectively.

Supravesical inguinal hernias

There were two such hernias, both in women. They were located in the mid-line. They had broad bases and their sizes were 5×6 cm and 6×3 cm respectively (Fig. 5). They extended inferiorly from the peritoneal cavity, posterior to the pubic symphysis. Both these hernias contained bowel.

DISCUSSION

Gullmo (1973; 1980) introduced the routine use of positive contrast herniography in adults. In an earlier series (Ekberg, 1980) we were able to demonstrate inguinal hernias in 46% of the men and 33% of the women with clinically unclear groin pain by the

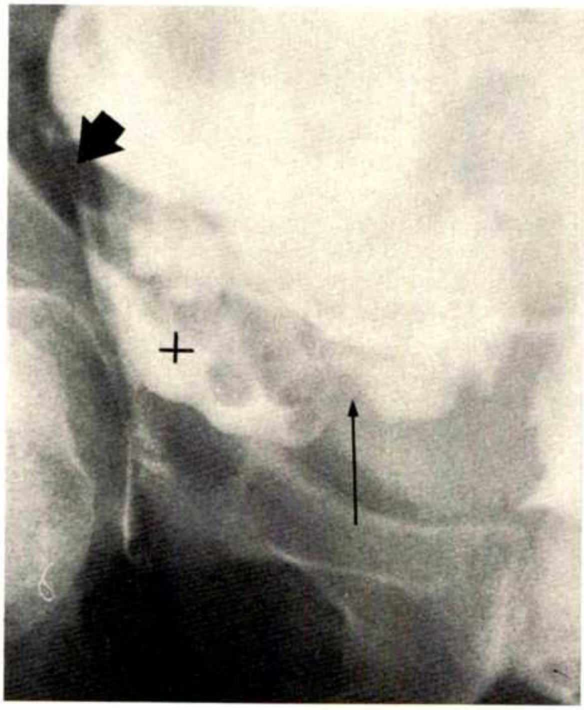


FIG. 1.

Direct inguinal hernia (+) located between the medial (thin arrow) and the lateral (thick arrow) umbilical folds.

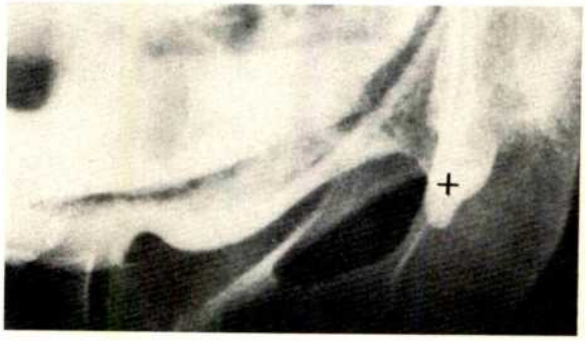


FIG. 2.

Inguinofemoral hernia (+).

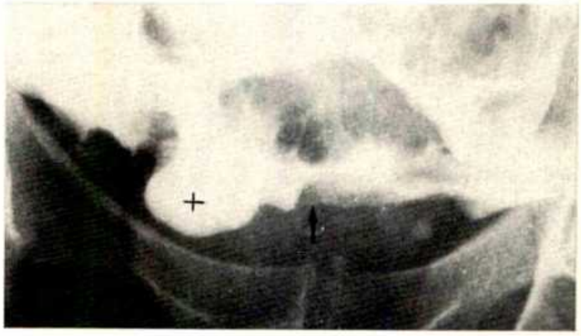


FIG. 3.

Medial direct inguinal hernia (+). Median (thin arrow) and medial (thick arrow) umbilical folds.

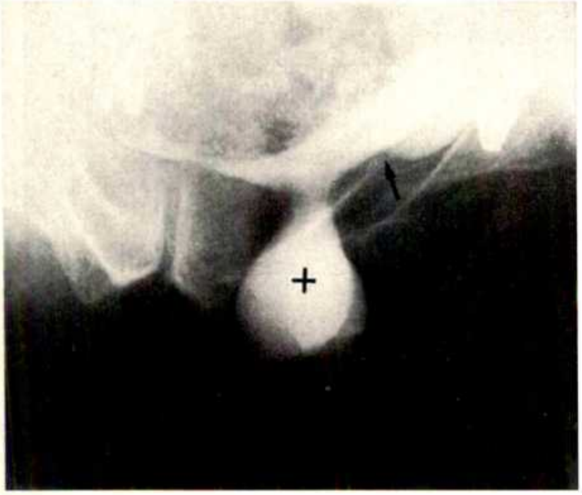


FIG. 4.
Diverticular direct inguinal hernia (+), protruding from the supravesical fossa. Medial umbilical fold (arrow).

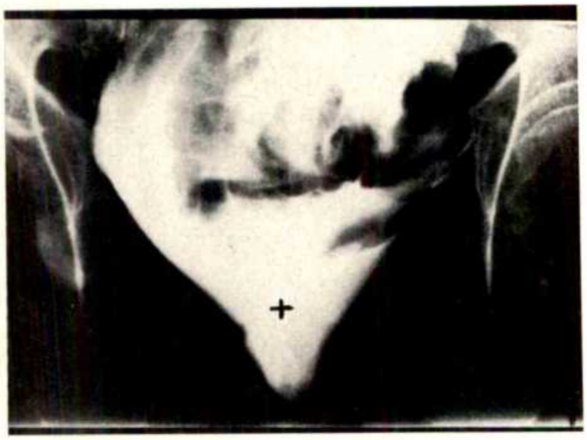


FIG. 5.
Supravesical inguinal hernia (+) protruding in the mid-line.

use of herniography. Thus, herniography revealed a probable cause of these patients' complaints. Herniography also enabled a pre-operative delineation of multiple hernias if present. As the examination is done with the inguinal structures undamaged by operation, a good description of the relation between the hernias and the different anatomical structures is possible which should facilitate the operative repair.

The wide spectrum of direct inguinal hernias has long been familiar to experienced surgeons (Nyhus and Harkins, 1964). With the introduction of herniography in adults it has been possible for the radiologists to identify some of these hernias.

The examination technique has been in use for several years in a paediatric age-group (Ducharme *et al.*, 1967; White *et al.*, 1968; Shackelford and McAlister, 1972; Oh *et al.*, 1973). The reason for performing herniography in infants has been to demonstrate or exclude the presence of a contralateral hernia when the history and/or physical examination indicate the presence of a unilateral inguinal hernia. The most frequent type of inguinal hernia in children is the indirect type. However, both femoral and direct types have been reported among children (Shackelford and McAlister, 1972; Oh *et al.*, 1978).

Indirect inguinal hernias are often referred to as congenital, as they are frequent in newborns and then decline in frequency with age. The importance of a patent processus vaginalis in relation to an indirect inguinal hernia has been extensively discussed (Sparkman, 1962; Leape, 1978; White *et al.*, 1968). In contrast to these, the direct inguinal hernias are often referred to as acquired. However, the aetiology of these direct hernias has also been claimed to be congenital in origin and to depend on a narrow rectus abdominis muscle, a weak transversalis fascia and a weak ileopectineus ligament (Fallis, 1938; Nyhus and Harkins, 1964).

The differentiation on the herniogram between the five types of direct inguinal hernias described above depends mainly on the identification of the median, medial and lateral umbilical folds. In this way the lateral hernias can be distinguished from the medial. The differentiation between a lateral and an inguinofemoral hernia is possible due to the fact that the latter hernia protrudes anteriorly and superiorly, while the inguinofemoral hernia protrudes inferiorly and somewhat anteriorly to the inguinal ligament. This means that the inguinofemoral hernias are better visualized on the straight PA views, while the lateral hernias are better visualized when the tube is angled caudally with the patient prone. Moreover, the inguinofemoral hernia is often smaller and has a more distinct neck than the lateral direct hernias. The inguinofemoral hernias can be distinguished from the true femoral hernias because the latter have narrow necks due to the rigidity of the femoral hernial orifice through which the hernias extend (Lytle, 1964).

The close relationship between direct and femoral hernias has been pointed out. Femoral hernias have been found to coexist with direct inguinal hernias in 28% of one series (Burton, 1960). This coexistence was found in only one of our patients. The anatomy in the inguinal region also favours the development of intermediary forms of these hernias as the intervening fascia transversalis constitutes the solitary barrier between direct and femoral hernias (Burton, 1964). Among the patients in this series with inguinofemoral hernias, the medial inguinal fossa was rather deep and from its inferior aspect there was a protrusion which extended inferiorly and slightly anteriorly. This could be explained by a weak fascia transversalis. The shape of the inguinofemoral hernia on the herniogram also made it probable that the apex of the hernia reached through the femoral ring into the femoral channel but not beyond the femoral hernial orifice (Lytle, 1964).

The shape of medial direct inguinal hernias is often rather similar to the lateral type, but they are sometimes more square. They protrude between the medial umbilical fold and the lateral border of the rectus abdominis muscle. This means that these patients should have a rather narrow rectus abdominis muscle, as the medial umbilical fold normally runs at the lateral edge of the muscle (Nyhus and Harkins, 1964; Fallis, 1938).

The diverticular type of direct inguinal hernias was found in two patients in this series. This type of hernia has been reported more frequently among operated patients (Burton and Blotner, 1941). One of our patients had had four hernioplasties. The diverticular hernias were both located in the medial aspect of the supravesical fossa and protruded anteriorly, probably through a weak rectus abdominis muscle. The narrow neck was typical of these hernias; they were also rather smaller than the other types in this series.

Supravesical hernias are located in the mid-line and protrude inferiorly and slightly anteriorly, whereby the median umbilical fold is effaced. These hernias have broad bases.

The presence of bowel or omentum in a peritoneal sac has been both claimed and denied to be a prerequisite for designating the sac a true hernia (Leape, 1978; White *et al.*, 1968). In this series loops of bowel and/or omentum were seen in 28 of 39 hernias. There was no correlation between the size of the hernias and whether or not they contained bowel or omentum. It may well be that the content of the hernia can slide in and out and that it is a matter of chance if it is in the peritoneal sac at the time of the herniography.

REFERENCES

Burton, C. C. and Blotner, C., 1941. Diverticular inguinal hernia. *Surgery, Gynecology and Obstetrics, 73*, 212–217.

Burton, C. C., 1960. Predictive criteria of preclinical femoral hernia. *Surgery, Gynecology and Obstetrics, 111*, 219–223.

1964. Important considerations in the repair of direct hernia. In *Hernia.* Ed. L. M. Nyhus and H. N. Harkins (Lippincott, Philadelphia), pp. 186–191.

Ducharme, J., Bertrand, R. and Chacar, R., 1967. Is it possible to diagnose inguinal hernia by X-ray? *Journal of the Canadian Association of Radiologists, 18*, 448–451.

Ekberg, O., 1981. Inguinal herniography in adults. *Radiology, 138*, 31–36.

Fallis, L. S., 1938. Direct inguinal hernia. *Annals of Surgery, 107*, 572–581.

Gullmo, Å., 1973. Herniografi. *Proceedings of the Swedish Society of Radiology, 2*, 19–20.

1980. Herniography. *Acta Radiologica, Supplementum* 361.

Leape, L. L., 1978. Herniograms—a commentary. *Surgery, 83*, 361–362.

Lytle, W. J., 1964. The low operation for femoral hernia. In *Hernia.* Ed. L. M. Nyhus and H. N. Harkins (Lippincott, Philadelphia), p. 208.

Nyhus, L. M. and Harkins, H. N., Eds., 1964. *Hernia.* (Lippincott, Philadelphia).

Oh, K. S., Dorst, J. P., White, J. J., Haller, J. A., Heller, R. M., James, A. E., Johnson, B. A. and Strife, J. L., 1973. Positive-contrast peritoneography and herniography. *Radiology, 108*, 647–654.

Oh, K. S., Condon, V. R., Dorst, J. P. and Grajo, G., 1978. Peritoneographic demonstration of femoral hernia. *Radiology, 127*, 209–211.

Shackelford, G. D. and McAlister, W. H., 1972. Inguinal herniography. *American Journal of Roentgenology, 115*, 399–407.

Sparkman, R. S., 1962. Bilateral exploration in inguinal hernia in juvenile patients. *Surgery, 51*, 393–406.

White, J. J., Parks, L. C. and Haller, J. A., 1968. The inguinal herniogram: a radiologic aid for accurate diagnosis of inguinal hernia in infants. *Surgery, 63*, 991–997.

1981, *British Journal of Radiology*, *54*, 500–504

Mean skeletal dose factors for beta-particle emitters in human bone. Part II: surface-seeking radionuclides*

By F. W. Spiers, C.B.E., D.Sc., Ph.D., F.Inst., P., †A. H. Beddoe, M.Sc., Ph.D., M. Inst.P. and Joan R. Whitwell, Ph.D.

Bone Dosimetry Research Unit, University of Leeds, Cookridge Hospital, Leeds LS16 6QB

(*Received August 1980 and in revised form January 1981*)

Abstract

Mean skeletal dose factors for surface-seeking β-emitting radionuclides have been derived on the basis of the β-particle dose factors calculated for human bones by Spiers *et al.* (1978b), or from empirical formulae representing these calculations given by Beddoe and Spiers (1979). The dose factors are derived for the same tissues as in Part I (Spiers *et al.*, 1978a), namely, (1), ${}_{S}\bar{D}_{M}/D_{\mathrm{skel}}$, the mean dose to haemopoietic marrow in trabecular bone, and (2), ${}_{S}\bar{D}_{S}/D_{\mathrm{skel}}$, the mean dose to endosteal tissues lying in a zone 0–10 μm from trabecular surfaces. The dose factors are given as fractions of D_{skel}, the "dose to bone", calculated from the energy released by the retained radionuclide divided by the total mass of mineral bone.

As in Part I, the dose factors are given for three ages, 1.7, 9 and 44 years and extrapolation to lower ages is made on the basis of calculations for a lumbar vertebra of an infant aged 3.5 weeks. The factors are given for six radionuclides covering a range of mean β-particle energies from 0.0255 MeV (^{171}Tm) to 0.93 MeV (^{90}Y).

The dosimetry is also considered for some radionuclides that first deposit on bone surfaces before being translocated to the bone volume. In the case of ^{45}Ca, for example, it is shown that the dose calculation that includes both the surface and the volume depositions gives integrated doses to ten days and 100 days that are respectively 4.5 and 1.9 times the corresponding values calculated conventionally on a volume deposition only. Endosteal dose factors are similarly considered, and other radionuclides included as surface-plus-volume depositions are ^{47}Ca, ^{89}Sr and ^{90}Sr + ^{90}Y.

In Part I of the paper under the above title (Spiers *et al.*, 1978a) mean skeletal dose factors were given for radionuclides distributed throughout the volume of the mineralized skeleton, and it is under this assumption that most calculations of dose to tissues in bone have hitherto been made. Consideration of the movement and redistribution of radionuclides in bone has been mainly in relation to the late effects of α emitters (see, for example, Jee (1972); Schlenker *et al.* (1976); Priest and Hunt (1979)), but interest centres also on β-emitting radionuclides used clinically, for some of these are first taken up by bone surfaces before becoming distributed in the bone volume. A quantitative model for the metabolism of the alkaline earth elements in man has been given by a task group of the International Commission on Radiological Protection (1972) and this takes account of both volume and surface retention. Data are given, for example, for calcium and, although the removal of calcium from bone surfaces may be fast compared with its long-term retention, a radioisotope of calcium may still deliver an appreciable fraction of its total dose during the initial period of deposition on bone surfaces.

Mean skeletal dose factors for surface-seeking β-emitting radionuclides have been derived, therefore, on the basis of the β-particle dose factors calculated for individual human bones by Spiers *et al.* (1978b), or from empirical formulae representing these calculations as given by Beddoe and Spiers (1979). The dose factors are derived for the same tissues as in Part I, viz. (1) the mean dose to active marrow and other mesenchymal cells in the marrow spaces and (2), the mean dose to endosteal tissues lying within a zone 0–10 μm from the trabecular surfaces (ICRP, 1977). The dose factors now reported give the ratios of the mean absorbed tissue dose-rate to the conventional "absorbed dose-rate to bone", calculated as the energy released by the retained radionuclide divided by the total mass of mineral bone. There is, however, a change in notation necessitated by the reference, in this case, to a surface deposition. For a uniform volume deposition the absorbed dose-rate to bone, D_{B}, is the same, whether calculated for a single bone or for the whole skeleton. This does not hold for surface-deposited radionuclides; in these calculations, a uniform deposition on all bone surfaces is assumed and the surface/volume ratio, S/V, is involved in calculating the conventional absorbed dose-rate to bone. The ratio S/V, however, varies with bone structure and is not the same for the skeleton as a whole as for any individual bone. Hence in this paper the notation D_{B} is reserved for any given bone and the notation D_{skel} is used for the dose-rate to the skeleton calculated from the total retained radionuclide divided by the mass of the mineral skeleton—quantities more likely to be known in a clinical situation than the retention and mass for an individual bone. The relationship between D_{skel} and D_{B} is that given by Spiers *et al.* (1978b):

---

*For Part I see The British Journal of Radiology, 1978, *51*, 622–627.

†Present address: Department of Medical Physics and Bioengineering, Auckland Hospital, Auckland, New Zealand.

$$D_{\mathrm{skel}}=\frac{D_{\mathrm{B}}(S/V)_{\mathrm{skel}}}{(S/V)_{\mathrm{B}}} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The mean skeletal dose factors given in this paper are then (1): ${}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}}$ and (2): ${}_{\mathrm{S}}\bar{D}_{\mathrm{S}}/D_{\mathrm{skel}}$ using the notation suggested by Marshall *et al.* (1978), modified as above.

The dose factors presented here are for the same three male subjects, aged respectively 1.7, 9 and 44 years, as those in Part I, and for the lumbar vertebra (LV3) of the child of 3.5 weeks (full gestational period). Calculations of the dose factors for surface-seeking radionuclides have been made for the same bones as in Part I and, in deriving the mean skeletal dose factors, the same weighting factors (and grouping of bones) have been used, as set out fully in Table I of the earlier paper. The dose factors have been calculated for six radionuclides known to be deposited partly or entirely on bone surfaces and chosen to provide, for purposes of computation, realistic β-particle spectra over a wide range of mean β-particle energies, from 0.0255 MeV to 0.927 MeV.

CALCULATION OF MEAN SKELETAL DOSE FACTORS

The dose factors ${}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}}$ and ${}_{\mathrm{S}}\bar{D}_{\mathrm{S}}/D_{\mathrm{skel}}$ in Table I, for individual bones of the 44 year-old man, have been derived from values of ${}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{B}}$ and ${}_{\mathrm{S}}\bar{D}_{\mathrm{S}}/D_{\mathrm{B}}$ given in Tables III and IV of the paper by Spiers *et al.* (1978b), modified by equation (1) to express the factors in terms of D_{skel}. For the 9 and 1.7 year-old children, the factors for individual bones have been calculated from the structural parameters of the bones using empirical formulae given by Beddoe and Spiers (1979) and similarly modified by equation (1). In the single case of the parietal bone for these two ages, the dose factors were obtained by extrapolation from the factors for other bones, because the empirical formulae did not hold for this rather extreme structure (very small marrow spaces and very thick trabeculae). In converting from D/D_{B} to D/D_{skel} a common value of $(S/V)_{\mathrm{skel}}=60.8\ \mathrm{cm}^{-1}$ was used for all age groups (Spiers *et al.*, 1978b).

Cortical contributions to the dose factors have been included as they were in Part I; they have been obtained on the assumption that radionuclides deposited on the surfaces of the cavities and periosteum of the cortex can be regarded as a uniform cortical distribution. The cortical contributions have then been interpolated, at the appropriate β-particle energies, from graphs of the cortical contributions previously calculated for volume seekers (Whitwell and Spiers, 1976). In this earlier publication, however, the cortical contributions were expressed in terms of $D_0=\rho D_{\mathrm{B}}$, where ρ is the ratio of mass stopping powers, soft tissue to bone, for the mean β-particle energy involved. The cortical contributions for the surface seekers were then calculated from the values for volume seekers, using the expression:

$$\underset{\text{(surface seeker)}}{\text{cortical contribution}}=\underset{\text{(volume seeker)}}{\text{interpolated value}}\times\rho\times\frac{(S/V)_{\mathrm{cortex}}}{(S/V)_{\mathrm{skel}}} \quad . \quad . \quad . \quad . \quad .(2)$$

The value of $(S/V)_{\mathrm{skel}}$ is taken as 60.8 cm^{-1} for all ages and $(S/V)_{\mathrm{cortex}}$ is taken as 28.5 cm^{-1} for the 44-year-old man and at the slightly lower value of 28.0 cm^{-1} for the two younger ages.

Equilibrium corrections have also been included, as in Part I, to allow for the escape of β-particle energy for the smaller-dimensioned bones. These corrections have been derived by interpolation from those used for the volume seekers.

Mean skeletal dose factors for each radionuclide were then calculated using the weighting factors set out in Table I of Part I.

MEAN SKELETAL DOSE FACTORS FOR AGES 1.7, 9 AND 44 YEARS

Values of the mean skeletal dose factors ${}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}}$ and ${}_{\mathrm{S}}\bar{D}_{\mathrm{S}}/D_{\mathrm{skel}}$ for the three ages are given in Table I for the six radionuclides listed together with their mean β-particle energies. In Figs. 1 and 2 the values of ${}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}}$ and ${}_{\mathrm{S}}\bar{D}_{\mathrm{S}}/D_{\mathrm{skel}}$ are plotted against the mean β-particle energy, $\bar{E}_{\beta}$, so that the dose factors for any radionuclide behaving as a surface-seeker can be found if $\bar{E}_{\beta}$ is known. The curves in Figs. 1 and 2 for the infant aged 0.067 year

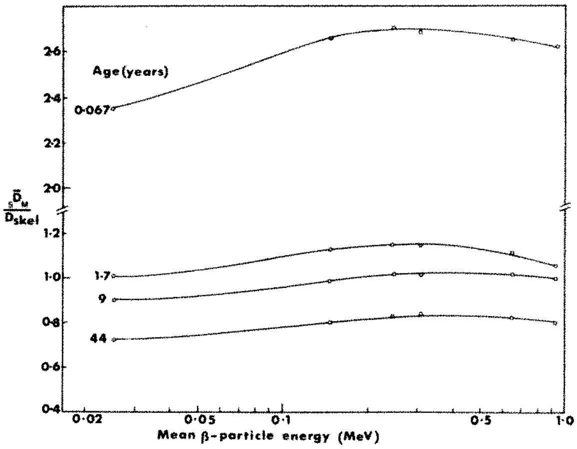


FIG. 1.

Variation of mean skeletal dose factors for marrow, ${}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}}$, with mean β-particle energy.

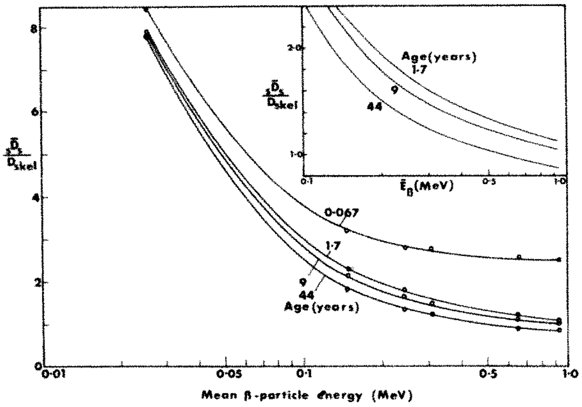


FIG. 2.

Variation of mean skeletal dose factors for endosteal tissues, ${}_S\bar{D}_S/D_{skel}$, with mean β-particle energy.

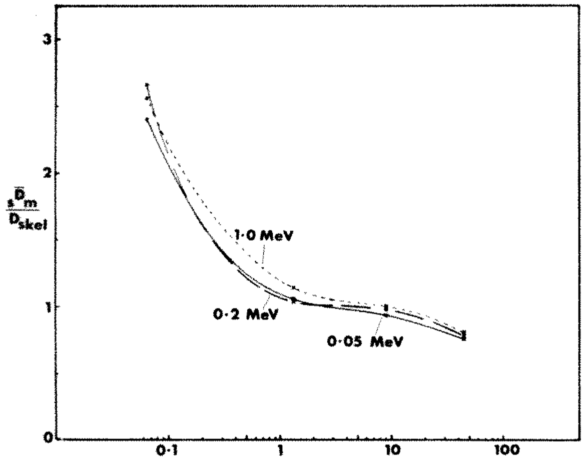


FIG. 3.

Variation with age of the mean skeletal dose factors for marrow, for three selected mean β-particle energies.

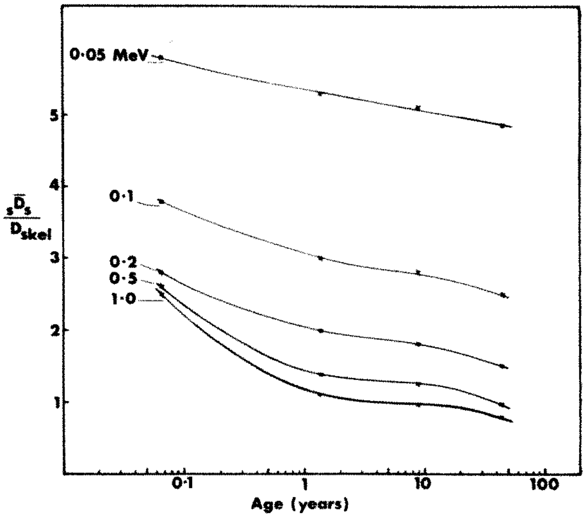


FIG. 4.

Variation with age of the mean skeletal dose factors for endosteal tissues, for five mean β-particle energies.

are approximate; they have been obtained as in Part I by extrapolation on the basis of the calculations for the lumbar vertebra, LV3. As in the case of the volume seekers, values of the mean skeletal dose factors for surface seekers are very close to those for the lumbar vertebra LV3. For the mean marrow dose factors, the values of the ratio ${}_S\bar{D}_M$(skeleton)/${}_S\bar{D}_M$ (LV3) for the six radionuclides lie in the range from 1.23 to 0.98 at age 44 years, from 1.18 to 0.99 at age 9 years, and from 1.03 to 0.95 at age 1.7 years; for the mean endosteal dose factors, all values of the corresponding ratio lie between 0.95 and 0.89. Extrapolation of the ratios for each radionuclide across the age range suggests that, at 0.067 year, the ratios for both the mean marrow and mean endosteal dose factors would be close to 0.90. Hence, the mean skeletal dose factors at the age 0.067 year can be taken as approximately those for the vertebra LV3, with an expected error not greater than 10%. In Figs. 3 and 4 the data have been recast to give values of ${}_S\bar{D}_M/D_{skel}$ and ${}_S\bar{D}_S/D_{skel}$ as functions of age for selected mean β-particle energies between $\bar{E}_\beta=0.05$ MeV and $\bar{E}_\beta=1.0$ MeV.

DISCUSSION

As discussed in Part I (Spiers *et al.*, 1978a) with reference to the volume-seeking radionuclides, the results given in this paper can reasonably be used for β-particle dosimetry in both sexes and the same reservations as to accuracy apply. Also the calculation of the value of D_{skel} is the same as that given in equations (3) and (4) of Part I, where the concentration C is the activity retained in the skeleton divided by the mass of the mineralized skeleton (formally 5 kg for the "reference man" (ICRP, 1976).

The results in this paper can be combined with those in Part I to investigate the effect of initial surface uptake on radionuclide dosimetry, at least in the case of some radionuclides of clinical interest—those of the alkaline earth series. Data on the retention functions for the series have been analysed and assembled by Marshall *et al.* in ICRP Report 20 (1972) and Fig. 5 is based on their results for calcium; it gives (1) the variation of uptake on bone surfaces with time (column 3 of Table 28 in that publication) and (2) the uptake in the bone volume

TABLE I

MEAN SKELETAL DOSE FACTORS FOR SIX SURFACE-SEEKING β-PARTICLE EMITTERS FOR SUBJECTS AGED 1.7, 9 AND 44 YEARS

Dose factor	Age (years)	Radionuclides and mean β-particle energies (MeV)					
		^{171}Tm 0.0255	^{115}In 0.147	^{204}Tl 0.241	^{143}Pr 0.308	^{70}Ga 0.648	^{90}Y 0.927
$\frac{{}_{\mathrm{S}}\bar{D}_{\mathrm{M}}}{D_{\mathrm{skel}}}$	1.7 9 44	1.002 0.895 0.727	1.123 0.984 0.795	1.144 1.011 0.821	1.142 1.012 0.823	1.105 1.008 0.816	1.048 0.990 0.792
$\frac{{}_{\mathrm{S}}\bar{D}_{\mathrm{S}}}{D_{\mathrm{skel}}}$	1.7 9 44	7.941 7.946 7.799	2.316 2.163 1.824	1.787 1.640 1.365	1.603 1.467 1.212	1.252 1.136 0.948	1.117 1.044 0.864

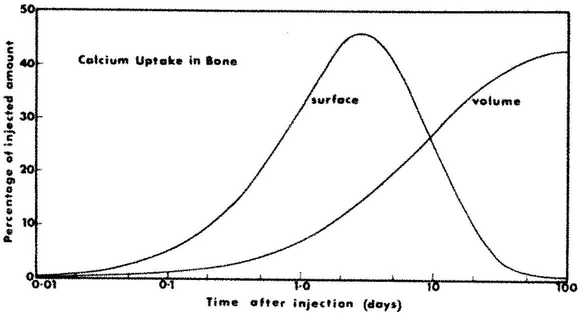


FIG. 5.

Variation of the percentage of the injected amount of calcium deposited on bone surfaces and in the bone volume with time after the injection (from data in ICRP Report 20, 1972).

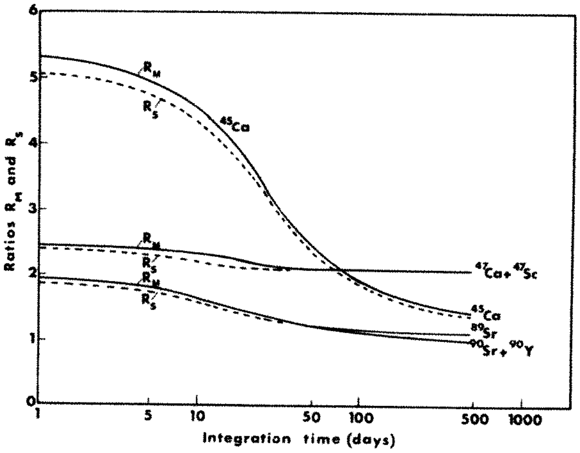


FIG. 6.

Values of the ratios, R_M and R_S, of the dose calculated for both surface and volume depositions to that calculated for volume deposition only. The ratios are given for dose-integration times up to 500 days post-injection.

(from the summation of data for compact and cancellous bone in columns 5–8 of the same Table). Similar data for other alkaline earth elements are also given in the ICRP Report. The values of the dose rates, D_{skel}, are proportional to these retentions, so that the variation of relative dose rate with time from both the surface and volume depositions can be calculated, with appropriate allowance for decay. If ${}_{\mathrm{S}}A$ is the activity on bone surfaces at any time and ${}_{\mathrm{V}}A$ that in the bone volume (ICRP Report 20, 1972), then the components of the total marrow dose rate are proportional to ${}_{\mathrm{S}}A({}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}})$ and ${}_{\mathrm{V}}A({}_{\mathrm{V}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}})$, where the factors in brackets are taken from Table I or Fig. 1 of this paper and Table II or Fig. 1 of Part I respectively, and the total marrow dose rate is proportional to their sum. If, however, all the retained activity, $({}_{\mathrm{S}}A+{}_{\mathrm{V}}A)$ were assumed to be volume-deposited, the corresponding marrow dose rate would be proportional to $({}_{\mathrm{S}}A+{}_{\mathrm{V}}A)\ ({}_{\mathrm{V}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}})$. The ratio R_{M} of the dose rate from the combined surface-plus-volume deposition to that usually calculated on the assumption of a purely volume deposition is then:

$$R_{\mathrm{M}}=\frac{{}_{\mathrm{S}}A({}_{\mathrm{S}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}})+{}_{\mathrm{V}}A({}_{\mathrm{V}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}})}{({}_{\mathrm{S}}A+{}_{\mathrm{V}}A)({}_{\mathrm{V}}\bar{D}_{\mathrm{M}}/D_{\mathrm{skel}})} \quad . \quad . \quad (3)$$

Values of the ratio R_{M} are shown by the solid lines in Fig. 6 for integrated doses over various times from one day to one year for the radionuclides ^{45}Ca, ^{47}Ca, ^{90}Sr $+^{90}$Y and ^{89}Sr. For ^{47}Ca the integration is for the β-ray doses from both ^{47}Ca and its decay product ^{47}Sc. It can be seen that, in the case of ^{45}Ca, the dose calculation that includes both surface and volume depositions gives integrated doses to ten and 100 days respectively as 4.5 and 1.9 times those calculated conventionally on a volume deposition only. For the short half-life isotope ^{47}Ca, the integrated dose calculated on a surface-plus-volume basis is from 2.4 to 2.1 times the conventional figure. The integrated doses for the two radioisotopes of strontium are only significantly greater than those calculated on a volume basis for integration times of less than about 50 days. Similar calculations for the corresponding ratio R_S for endosteal tissue doses yield values only slightly different from those for the mean marrow doses, as indicated by the dotted curves in Fig. 6. Although corresponding metabolic data are not yet available for other radionuclides, these results for the radioisotopes of calcium and strontium suggest that there may be some circumstances in the clinical use of radionuclides where bone-surface deposition, as well as the conventionally used bone-volume deposition, should be taken into account in dosage calculations.

ACKNOWLEDGMENT

This work was carried out with the support of the Medical Research Council.

REFERENCES

BEDDOE, A. H. and SPIERS, F. W., 1979. A comparative study of the dosimetry of bone-seeking radionuclides in man, rhesus monkey, beagle and miniature pig. *Radiation Research, 80*, 423–439.

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, 1972. Alkaline earth metabolism in adult man. *ICRP Publication No. 20* (Pergamon Press, Oxford).

1976. Reference man: anatomical, physiological and metabolic characteristics. *ICRP Publication No. 23* (Pergamon Press, Oxford).

1977. Recommendations. *ICRP Publication No. 26* (Pergamon Press, Oxford).

JEE, W. S., 1972. Distribution and toxicity of plutonium-239 in bone. *Health Physics, 22*, 583–595.

MARSHALL, J. H., GROER, P. G. and SCHLENKER, R. A., 1978. Dose to endosteal cells and relative distribution factors for radium-224 and plutonium-239 compared to radium-226. *Health Physics, 25*, 91–101.

PRIEST, N. D. and HUNT, B. W., 1979. The calculation of annual limits of intake of plutonium-239 in man using a bone model which allows for plutonium burial and recycling. *Physics in Medicine and Biology, 24*, 547–558.

SCHLENKER, R. A., OLTMAN, B. G. and CUMMINS, H. T., 1976. Microscopic distribution of plutonium-239 in bone from a human injection case. In *The Health Effects of Plutonium and Radium*, Ed. by W. S. Jee (J. W. Press, Salt Lake City, Utah), pp. 321–328.

Book reviews

Single Photon Emission Computed Tomography and other Selected Computer Topics. Co-ordinated by J. A. Sorenson, pp. 244, 1980 (Society of Nuclear Medicine, New York), $27.00.
ISBN 0–932004–06–07

This book contains the papers which were presented at the Tenth Annual Symposium on the Sharing of Computer Programs and Technology in Nuclear Medicine, held in Miami Beach in January, 1980, sponsored by the Computer Council of the Society of Nuclear Medicine.

Rapid publication of this paperback has been achieved as a result of the manuscripts being prepared by the separate authors in camera-ready form. The papers are clearly presented, and the images and illustrations are of high quality. However, there is no index, and none of the discussions at the symposium have been presented.

The first 14 of the 21 papers are concerned with single-photon emission computed tomography. After an excellent overview of the subject in the first paper, two review papers describe the alternative methods of image reconstruction for transaxial emission computed tomography. Unfortunately, these two papers devote little attention to the important problem of photon attenuation, the correction for which is essential for quantitative single-photon emission tomography. The remaining papers in the first section of the book describe the performance of the many systems which are available for imaging either transverse or longitudinal sections of the body. Greater emphasis has been given to the more recent longitudinal-section instruments which comprise a gamma-camera with a multiple pinhole or slant hole collimator. Comparisons have been made of the performance specifications of some of these instruments.

A selection of different computer topics is discussed in the final seven papers of the book. Three of these papers deal with the analysis of cardiac studies, including the use of the temporal Fourier transform. The others deal with data acquisition, data storage, deadtime problems and whole-body counting.

Most of the papers concerning transaxial emission tomography contain information which has already appeared elsewhere in the literature. However, this forms a small proportion of the book and the other papers present data which is new. This book will be of interest to physicists and computer specialists concerned with the application of computers in nuclear medicine, and provides an up-to-date overview of the current status of single-photon emission computer tomography.

M. A. FLOWER.

Grenz Rays. An Illustrated Guide to the Theory and Practical Application of Soft X rays. By D. Graham and J. Thomson, pp. x+149, 1980 (Pergamon Press, Oxford), £10·00.
ISBN 0–08–025525

This little book describes in great detail how to use very low energy X rays for several kinds of investigation. The authors have used a Gillardoni unit with a beryllium window, mostly between 5 and 20 kV. At these energies conventional films cannot be used in envelopes or cassettes; instead special fine-grain industrial films are used with the object in contact with the film.

The authors' main experience is in the forensic field. The book is profusely illustrated; the pictures of forged bank notes, altered cheques and envelopes steamed open and resealed are particularly fascinating. Finger prints can be reproduced after dusting with lead the surface of a thin sheet bearing the incriminating marks.

The other examples of the use of Grenz rays have a lesser immediate impact but include finely detailed radiographs of plants, insects and paintings. A chapter on mammography is a little surprising as the kV used is so much higher and the technique is in much more common use.

The book performs a valuable service in drawing attention, in an enjoyable way, to the many uses of radiography with very soft X rays.

D. K. BEWLEY.

1981, *British Journal of Radiology*, *54*, 505–511 JUNE 1981

The effect of dexamethasone on the radiation survival response and misonidazole-induced hypoxic-cell cytotoxicity in Chinese hamster cells V-79-753B *in vitro*

By Barbara C. Millar, Ph.D. and Sally Jinks, H.N.C.

Radiobiology Group, Institute of Cancer Research, Sutton, Surrey

(*Received November 1980 and in revised form January 1981*)

ABSTRACT

Overnight exposure of Chinese hamster cells, V-79-753B, to microgram quantities of the synthetic corticosteroid, dexamethasone, resulted in a decrease in sensitivity towards radiation, both in air and in hypoxia. The effect was dose-modifying and the oxygen enhancement ratio did not change appreciably. Similarly, when dexamethasone-treated hypoxic cells were irradiated in the presence of misonidazole, a hypoxic cell radiosensitizer, there was a decrease in radiation sensitivity compared with untreated hypoxic cells irradiated with misonidazole. The effect of dexamethasone cannot be attributed to classical radioprotection since administration of the drug immediately or 4.5 h before irradiation does not alter the survival response of hypoxic cells with or without misonidazole. Neither can this increased radioresistance be attributed to synchronization to a more resistant phase of the cell cycle since pretreated cells remain more radioresistant for at least 6 h after the removal of the drug. The data suggest that dexamethasone induces metabolic changes in cells which alter their radiosensitivity. Whatever metabolic changes may be occurring there was no effect on the uptake of ^{14}C-misonidazole into dexamethasone-treated or control cells. However, there was a pronounced decrease in hypoxic-cell cytotoxicity induced by misonidazole in cells pretreated with dexamethasone. The implications of these results are discussed.

The possibility that hypoxic cells in tumours may form foci for regrowth after fractionated radiotherapy is well established. Misonidazole, a 2-nitroimidazole, has been shown to sensitize selectively hypoxic mammalian cells both *in vitro* (for review see Adams *et al.*, 1978) and *in vivo* (Denekamp and Harris, 1975); clinical trials are in progress to determine whether the drug is likely to provide any therapeutic advantage in radiotherapy regimes (Dische *et al.*, 1977; Urtasun *et al.*, 1977; Jentzch *et al.*, 1977; Bleehen, 1980). Misonidazole has also been shown to be cytotoxic towards hypoxic mammalian cells *in vitro* (Hall and Roizin-Towle, 1975) and to potentiate the effects of other chemotherapeutic agents both *in vitro* (Stratford *et al.*, 1980) and *in vivo* (Rose *et al.*, 1980). Thus, this compound is potentially useful as an adjuvant to chemotherapy as well as radiotherapy.

Despite the possible advantages of including misonidazole in cancer treatments, its use in the clinic is limited by neurotoxicity (Dische *et al.*, 1977; Urtasun *et al.*, 1977). However, a recent report (Wasserman *et al.*, 1980) has indicated that this neurotoxicity is reduced in patients given dexamethasone before receiving misonidazole.

Dexamethasone is a synthetic corticosteroid which is widely used clinically for the treatment of cerebral oedema (see Martindale: *The Extra Pharmacopœia*, 1976). The effects of steroids at the cellular level vary according to the tissue of origin and the availability of cellular receptor sites. In general, steroids are inducers of synthesis of protein, DNA and all the major classes of RNA (Thompson, 1976). However, not all of these effects are seen in all tissues. The differentiated nature of various cell types determines whether they respond to steroids at all and in particular to which steroids and with which response.

The present series of experiments was undertaken as a preliminary study to investigate whether dexamethasone changes the radiation response of cells *in vitro* and whether the ability of misonidazole to kill hypoxic cells selectively is changed after exposure to dexamethasone. The ultimate aim from such work is an attempt to predict the underlying mechanism whereby dexamethasone protects against neurotoxicity in man and whether the therapeutic gain likely to be achieved by using misonidazole will be lost in patients given dexamethasone.

MATERIALS AND METHODS

Compounds

Misonidazole and 2-^{14}C-misonidazole (1.98 MBq or 53.6 μCi/mg) were kindly supplied by Roche Products Limited. Dexamethasone disodium phosphate was a gift from Merck, Sharp and Dohme (Hoddesdon, Herts, UK).

Cell culture

Chinese hamster V-79-753B cells were used throughout the work. The routine handling of cells was carried out using methods described previously (Cooke *et al.*, 1976).

For experiments involving the pretreatment of cells with dexamethasone, 110 g (4 oz) glass medical flats containing 6×10^5 cells/bottle were seeded the day preceding the experiment. When the cells had attached to the glass the medium was changed for similar growth medium containing dexamethasone at the required concentration. The medium on control cells was also replaced at the same time for fresh growth medium. On the day of the experiment, cells were trypsinized and harvested as a single cell suspension into medium with or without dexamethasone as required. Overnight exposure of cells to dexamethasone did not affect their gross morphology, neither did it inhibit cell division. The doubling time of cells exposed to 20 μg/ml dexamethasone was similar to that for untreated cells, but there was an increase in the doubling time of cells exposed to 50 μg/ml or 100 μg/ml from 9.5 h to 12 h. Cells were plated onto 61 mm glass petri dishes and allowed to attach at 37°C.

Irradiation procedure

Before irradiation the medium was aspirated from the dishes and replaced with 0.5 ml/dish of similar medium with or without dexamethasone and/or misonidazole. Triplicate samples for each radiation dose were placed in prewarmed (37°C) "Dural" irradiation containers (Cooke *et al.*, 1980). For experiments in hypoxia the containers were flushed with O_2-free N_2 (BOC$<$ 10 ppm O_2) for 15 min before irradiation. The gas was wetted by bubbling through distilled water at 37°C, to prevent the cultures from drying. During the gassing procedure, cultures were maintained at 37°C on a temperature-controlled plate. After gassing, the inlet and outlet valves of the containers were sealed to maintain hypoxia. Irradiation was carried out at 37°C using a ^{60}Co source and a dose rate of 5.0 Gy min^{-1}. After irradiation the medium was aspirated from the dishes and replaced with 2.0 ml of fresh growth medium.

Cytotoxicity

Cells were seeded and cultured as described above. Control cultures and dexamethasone-treated cultures were maintained in hypoxia for the times indicated in the text. The volume of medium on each dish was 2.0 ml to prevent loss by evaporation during the prolonged gassing time (up to 6 h). The medium was changed for 2.0 ml fresh growth medium at the end of the exposure to hypoxia.

Colony formation

Cultures were incubated at 37°C for six days in air containing 5% CO_2 to allow colony formation. The colonies were then fixed with ethanol, stained with methylene blue and counted. All irradiation data were taken from full survival curves. Each experiment consisted of a control curve for hypoxic cells, a control curve for hypoxic cells treated with dexamethasone, a curve for untreated hypoxic cells in the presence of misonidazole or untreated aerobic cells, and a curve for dexamethasone-treated hypoxic cells in the presence of misonidazole or dexamethasone-treated aerobic cells. This allowed comparison of data on a "same day" basis as well as between separate experiments. Both radiation survival and cytotoxicity experiments were done at least twice.

Computer analysis

Pooled data were analysed by computer CCDC 6400 (Millar *et al.*, 1978) to fit the multitarget equation. This was done to remove subjective bias and not as a means of interpreting the underlying mechanism(s). The values obtained by computer fit were fed into a second programme (unpublished) which gave theoretical curves for the survival parameters. Some of these curves are shown in the figures with the observed data points superimposed.

Labelling experiments

1.3×10^6 cells V-79-753B were seeded into each of four 110 g (4 oz) medical flats. The procedure for dexamethasone treatment was as above. Two bottles were given dexamethasone and two left as controls. On the day of the experiment cells were harvested into similar media, counted using a Coulter counter (industrial model D) and pelleted in an MSE bench centrifuge at 800 r.p.m. for 5 min. The cell pellets were resuspended in 2.5 ml of medium with or without dexamethasone and containing 150 kBq (4 μCi)/ml 2-^{14}C-misonidazole and 1.0 mM unlabelled misonidazole. The cell suspensions were incubated at 37°C for 1 h with occasional shaking. At this time the cells were pelleted as above and resuspended in 0.2 ml of similar media also containing 1.0 mM misonidazole but without label. The cells were pelleted through oil (silicone fluid : mineral oil; 4 : 1 (Dimethicone 20, Midland Silicone; 3 in one, E. R. Howard Ltd, Ipswich)) (Redwood and Colvin, 1980) in a Burkard 320a micro-centrifuge for one minute, to remove extracellular water. The resultant cell pellets were dissolved in 0.5 ml Protosol (New England Nuclear, Boston, Mass., USA) which was added to 9.5 ml Scintillator 299 (Packard, Illinois, USA). An aliquot of each of the labelled media (0.1 ml) was added to a similar scintillation mixture. Samples were allowed to cool for one hour before counting the ^{14}C activity in an Intertechnique SL3000 scintillation counter.

The uptake of 2-^{14}C-misonidazole was calculated from the counts in the cells compared with those in the medium. The following calculation was used to determine the percentage drug uptake (Brown, unpublished):

cell volume $= 4\pi r^3/3$ where $r =$ radius of cell ($7.5\,\mu$m)

$$\therefore \text{ cell volume} = 4\pi (7.5)^3/3\ \mu\text{m}^3$$

$$\therefore \text{ volume of } 10^6 \text{ cells} = 1.767 \times 10^{-3} \text{ ml}$$

$$\therefore \text{ counts/ml in cell pellet} = \text{c.p.m.} \times 10^3/1.767$$

$$\therefore \%\ \text{drug uptake} = \frac{\text{c.p.m./ml in cells}}{\text{c.p.m./ml in medium}} \times 100.$$

RESULTS

The data in Fig. 1 show the effect of 50 μg/ml dexamethasone on the radiation response of the cells irradiated in air or in hypoxia. The drug was present for about 20 h before and during irradiation. Whilst there was no appreciable change in the oxygen enhancement ratio (OER) there was a considerable increase in the D_0 values in air and in hypoxia. The computed data in Table I show that dexamethasone increased by about 25% the radiation dose required to produce a given amount of cell killing. A similar increase in D_0 was seen when dexamethasone-treated hypoxic cells were irradiated in the presence of 1.0 mM misonidazole. The misonidazole was given 15 min before irradiation and dexamethasone was also present during irradiation (Fig. 2). The computed values for these experiments are also shown in Table I. Data to show that misonidazole does not sensitize aerobic cells treated with dexamethasone are shown in Table I for comparison.

The possibility that dexamethasone may be acting as a classical radioprotector was investigated by giving the drug (50 μg/ml) 15 min before irradiation in hypoxia with or without 1.0 mM misonidazole. The computed survival parameters for these experiments are shown in Table II. There was no appreciable change in either the hypoxic radiation response or the response of hypoxic cells irradiated in the presence of 1.0 mM misonidazole when dexamethasone was given immediately before irradiation.

A second possibility is that dexamethasone may arrest cells in a more resistant phase of the cell cycle. Cultures were incubated with 50 μg/ml of dexamethasone overnight. At the time of plating the cells were washed free of the drug. Irradiation was carried out 5.5–6 h after the removal of dexamethasone, in

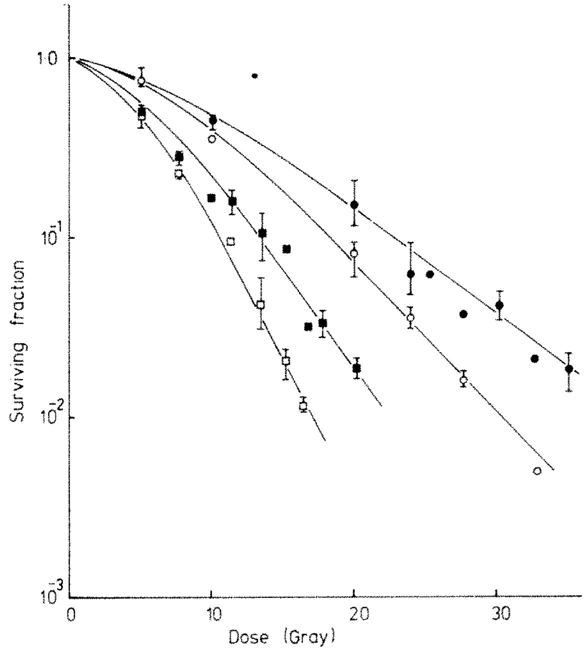


FIG. 1.

Effect of pretreatment of Chinese hamster cells V-79-753B with 50 μg/ml dexamethasone for 20 h before and during irradiation in air or in hypoxia at 37°C; ○, control cells/N_2; ●, dexamethasone-treated cells/N_2; □, control cells/air; ■, dexamethasone-treated cells/air. In each figure error bars denote the range of data points from pooled experiments.

TABLE I

THE EFFECT OF PRETREATMENT OF CHINESE HAMSTER CELLS V-79-753B WITH 50 μg/ml DEXAMETHASONE FOR 20 h BEFORE IRRADIATION

Conditions	Control cells			Dexamethasone-treated cells			Ratio
	D_0 Gy	n	ER	D_0 Gy	n	ER	D_0 (control) / D_0 (dexamethasone)
N_2	5.40 ± 0.21	2.97 ± 0.54	1.0	7.01 ± 0.44	2.15 ± 0.47	1.0	0.77
Air	1.95 ± 0.10	3.65 ± 0.89	2.77	2.70 ± 0.13	3.23 ± 0.83	2.63	0.72
1.0 mM misonidazole/N_2	2.97 ± 0.15	3.71 ± 0.85	1.82	4.04 ± 0.17	2.81 ± 0.40	1.74	0.74
1.0 mM misonidazole/air	1.93 ± 0.16	3.35 ± 0.7	2.80	2.75 ± 0.08	3.33 ± 0.24	2.56	0.70

TABLE II

The effect of giving 50 μg/ml dexamethasone to Chinese hamster cells V-79-753B 15 min or 4.5 h before irradiation in hypoxia with or without 1.0 mM misonidazole

Conditions	Control cells			Dexamethasone present 15 min b.i.*			Dexamethasone present 4·5 h b.i.		
	D_0 Gy	n	ER	D_0 Gy	n	ER	D_0 Gy	n	ER
N_2	5.40±0.21	2.97±0.54	1.0	5.65±0.38	3.56±1.03	1.0	5.42±0.60	3.34±0.73	1.0
1.0 mM misonidazole/N_2	2.97±0.15	3.71±0.81	1.82	2.94±0.35	3.5 ±0.9	1.92	2.86±0.13	3.97±1.04	1.89

*b.i. = before irradiation.

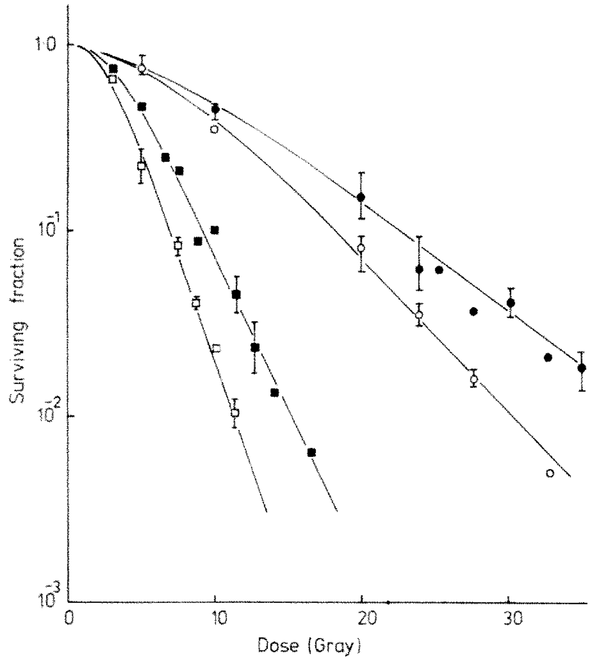


Fig. 2.

Effect of pretreatment of Chinese hamster V-79-753B cells with 50 μg/ml dexamethasone for 20 h before and during irradiation in hypoxia in the presence of 1.0 mM misonidazole at 37°C; O, control cells/N_2; ●, dexamethasone-treated cells/N_2; □, control cells with 1.0 mM misonidazole; ■, dexamethasone-treated cells with 1.0 mM misonidazole.

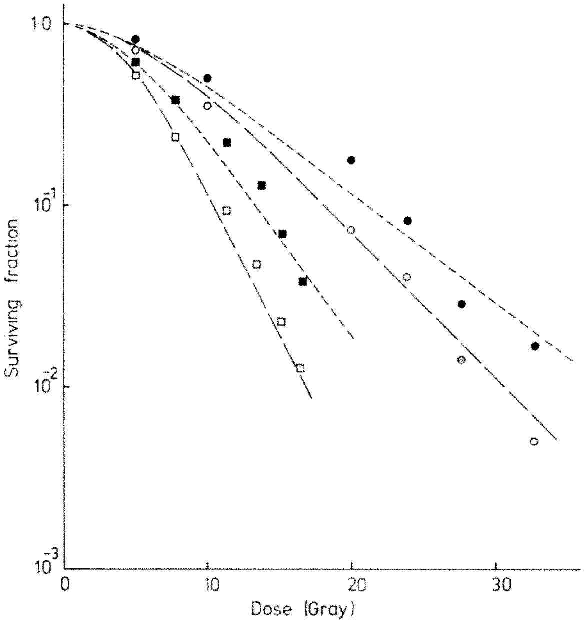


Fig. 3.

Effect of 1.0 mM misonidazole on the radiation response of Chinese hamster cells V-79-753B which were pretreated for 16 h with 50 μg/ml dexamethasone and washed free of dexamethasone 6 h before irradiation in hypoxia at 37°C; O, control cells/N_2; □, 1.0 mM misonidazole with control cells; ●, control dexamethasone-treated cells/N_2; ■, dexamethasone-treated cells with 1.0 mM misonidazole.

hypoxia with or without 1.0 mM misonidazole. The data from these experiments are shown in Fig. 3. The radiation response of the dexamethasone-treated cells remained unchanged after the drug had been removed for 5.5–6 h. Additionally, when cells were given dexamethasone for 4.5 h before irradiation the survival response of hypoxic cells and of hypoxic cells irradiated in the presence of 1.0 mM misonidazole was similar to that for untreated cells (Table II).

In view of the fact that dexamethasone is a synthetic hormone, a further series of experiments was carried out to determine whether the concentration of dexamethasone used to pretreat cells affected the degree of change seen in the hypoxic radiation survival response. Cells were treated with dexamethasone at concentrations of 5, 20, 50 and 100 μg/ml as before. Irradiation was carried out when the dexamethasone had been present for 20 h. The

TABLE III

THE EFFECT OF PRETREATMENT OF CHINESE HAMSTER CELLS WITH DIFFERENT CONCENTRATIONS OF DEXAMETHASONE FOR 20 h BEFORE IRRADIATION IN HYPOXIA

Concentration of dexamethasone (μg/m)	D_0	n	D_0 control D_0 (dexamethasone)
0.0	4.96 ± 0.06	3.93 ± 0.3	1.0
5.0	5.96 ± 0.34	2.86 ± 0.70	0.83
20.0	6.67 ± 0.35	2.87 ± 0.57	0.74
50.0	6.61 ± 0.33	2.54 ± 0.54	0.75
100.0	6.65 ± 0.31	2.71 ± 0.35	0.75

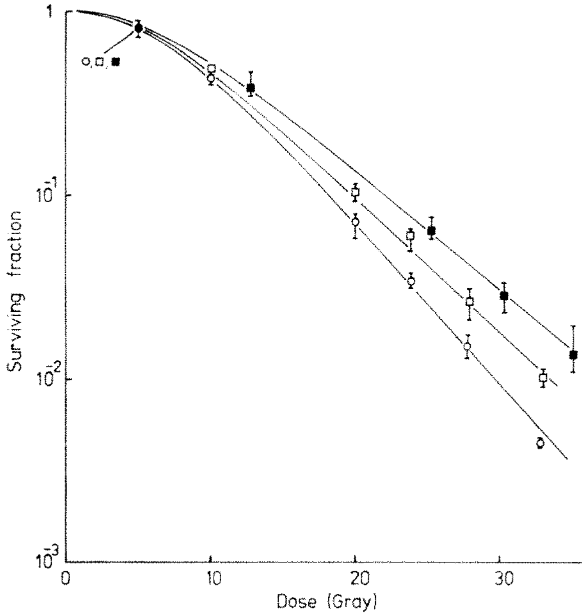


FIG. 4.

Effect of pretreatment of Chinese hamster cells V-79-753B with different concentrations of dexamethasone for 20 h before irradiation in hypoxia; O, control cells; □, cells treated with 5 μg/ml dexamethasone; ■, cells treated with 20, 50 or 100 μg/ml dexamethasone.

results are shown in Fig. 4 and the computed values in Table III.* With concentrations of dexamethasone between 20 and 100 μg/ml there was a constant degree of radioprotection of hypoxic cells. An intermediate amount of protection was seen in cells pretreated with 5 μg/ml dexamethasone. When cells are treated with hydrocortisone for a similar length of time there is no change in the radiation response of hypoxic or aerobic Chinese hamster V-79-753B cells for the same concentration range (Millar, unpublished). This may be because dexamethasone is a much more potent corticosteroid than hydrocortisone, and a higher concentration may be required to change the radiation response of cells.

It was of interest to investigate whether pretreatment with dexamethasone affects the ability of misonidazole to induce hypoxic-cell cytotoxicity. Cells which had been treated with 50 μg/ml dexamethasone for 16 h were maintained in hypoxia for up to 6 h in the presence of 10 mM misonidazole. Untreated cells were also maintained in medium containing 10 mM misonidazole for similar lengths of time. The data are shown in Fig. 5. Pretreatment with dexamethasone protected cells from the cytotoxic effects of misonidazole. After 6 h in hypoxia, cell survival was reduced to 3.7% for untreated cells compared with 31% for dexamethasone-treated cells. Protection by dexamethasone against toxicity of misonidazole in hypoxic cells has also been seen in a mouse fibrosarcoma cell line, HSDM$_1$C$_1$ (Millar, unpublished).

This protection may be due to a change in the uptake of misonidazole in dexamethasone-treated cells. The intracellular concentration of 2-^{14}C-misonidazole was examined in cells that had been pretreated with 50 μg/ml dexamethasone compared with untreated cells. The concentration of misonidazole in control cells was 24.5% of that found in the medium compared with 29.6% for cells treated with dexamethasone after a 1 h incubation period.

DISCUSSION

The data provide evidence that dexamethasone may cause biochemical changes in cells which result in a change in their radiation response. Chinese hamster V-79-753B cells which had been exposed to dexamethasone (50 μg/ml) for about 20 h before irradiation were significantly more radiation-resistant in air and in hypoxia than untreated cells. Whilst there was no appreciable change in the OER, the dose of radiation required to produce a given amount of cell killing had to be increased by approximately 25%. This increase in radiation-resistance after dexamethasone treatment was similar for cells given 20–100 μg/ml of the drug for 20 h before irradiation.

---

*Since the data points for concentrations between 20 and 100 μg/ml of dexamethasone were very close together the mean value of each survival point has been plotted in Fig. 4 for experiments using these drug concentrations. The error bars show the range of data over this range of dexamethasone concentration. The computed values (Table III) show the actual survival parameters for each concentration of dexamethasone.

Dexamethasone did not behave as a classical radioprotector since there was no increase in radiation resistance when cells were given the drug immediately before irradiation. Neither can it be argued that dexamethasone arrests cells at a more resistant phase of the cell cycle since the enhanced radiation resistance was detectable 6 h after the cells had been washed free of dexamethasone. Additionally, the drug had to be present for a considerable time (>5 h) before there was any change in the radiation response compared with that of untreated cells.

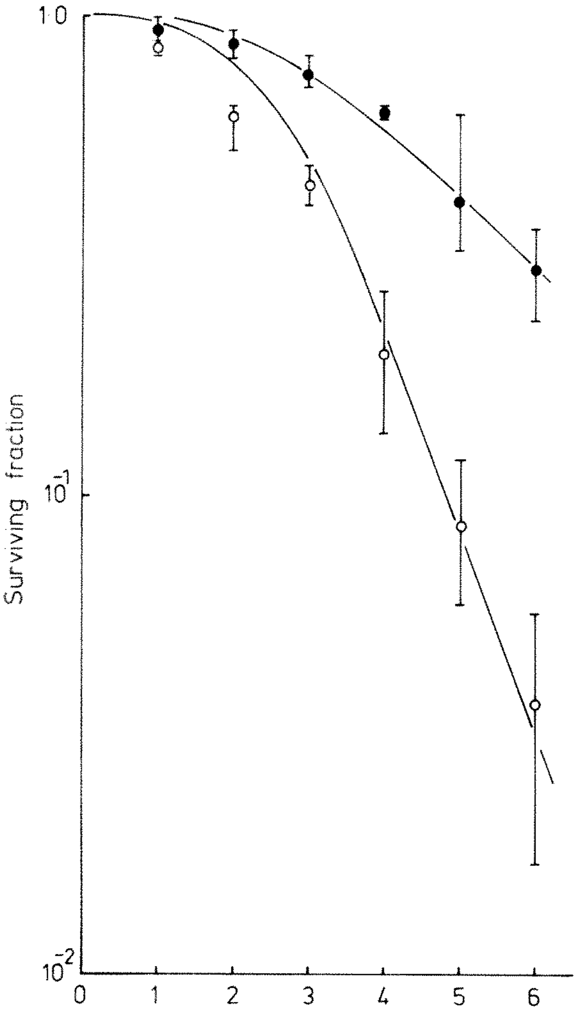


Fig. 5.

Effect of pretreatment of Chinese hamster cells V-79-753B with 50 μg/ml dexamethasone for 20 h on the hypoxic-cell cytotoxicity induced by 10.0 mM misonidazole; ○, control cells with 10.0 mM misonidazole; ●, dexamethasone-treated cells with 10.0 mM misonidazole.

When dexamethasone-treated hypoxic cells were irradiated in the presence of 1.0 mM misonidazole the enhancement ratio was about 1.9, similar to that for untreated hypoxic cells irradiated in the presence of the sensitizer. However, there was an increase in D_0 from 2.97 Gy (untreated cells) to 4.04 Gy (dexamethasone-treated cells). Thus, whilst the efficiency of the sensitizer did not change, the data suggest that the absolute amount of cell killing was determined by the metabolic state of the cells.

In other systems there is evidence that corticosteroids induce membrane changes. Dexamethasone has been shown to increase adhesiveness in a line of rat hepatoma cells (HTC) *in vitro* (Ballard and Tomkins, 1970), and this has been attributed to changes in the cell membrane analogous to reverse transformation (Gelehrter, 1976). Similar changes in gross morphology and surface microvilli have been seen after treatment with glucocorticoids in a heteroploid line of normal rat liver cells (Berliner, 1975). It has yet to be shown for Chinese hamster cells V-79-753B that the decreased radiation sensitivity can be attributed to membrane changes. However, there is evidence *in vivo* that dexamethasone decreases lysosomal activity in nerve cells (Clarke—personal communication).

Dexamethasone treatment also protected Chinese hamster V-79-753B cells from hypoxic-cell cytotoxicity caused by misonidazole. This could not be accounted for on the basis of a change in uptake of misonidazole since labelling experiments showed a similar degree of incorporation into control and dexamethasone treated cultures. Experiments *in vivo* have shown that dexamethasone does not alter the blood pharmacokinetics, nor the rate of demethylation of misonidazole *in vivo*. However, there is a small but significant decrease in the peak brain concentration and the area under the curve in animals given dexamethasone before misonidazole (Workman, 1980).

Glucocorticoids have been shown to induce the synthesis of specific enzymes (Kenney, 1962; Thompson, 1976) as well as to exert effects on cell membranes. Thus it is possible that the observed decrease in cytotoxicity may be due both to changes in membrane stability and also in the cell's enzymatic complement which may influence drug metabolism and/or intracellular distribution.

It is unlikely that dexamethasone will induce similar biochemical changes in all cell types in man since not all cells will possess the necessary receptors for hormone action. Preliminary data *in vivo* have shown that dexamethasone does not change the radiation response of the CFU-S compartment of the bone marrow. However, further investigations are essential to determine whether tumour cells are protected by dexamethasone treatment. This will be necessary in order to evaluate whether the therapeutic gain likely to be achieved by misonidazole will be lost when this corticosteroid is included in radiotherapy or chemotherapy regimes.

ACKNOWLEDGMENTS

Sincere thanks are given to Mr. J. Currant for technical assistance and to Professor G. E. Adams and Drs. T. J. Powles and E. M. Fielden for their helpful discussion. This work was supported by the MRC/CRC.

REFERENCES

ADAMS, G. E., FOWLER, J. F. and WARDMAN, P. Ed. 1978. Hypoxic cells in radiobiology and radiotherapy. *British Journal of Cancer*, *37*, Supplement III.

BALLARD, P. and TOMKINS, G. M., 1970. Glucocorticoid induced alteration of the surface membrane of cultured hepatoma cells. *Journal of Cellular Biology*, *47*, 222–234.

BERLINER, J. A., 1975. *Gene Expression and Carcinogenesis in Cultured Liver* (Academic Press, New York), p. 181.

BLEEHEN, N., 1981. Clinical studies with misonidazole; results of a trial in glioblastoma multiforme. *Proceedings of the Conference on Combined Modality Cancer Treatment: Radiation Sensitizers and Protectors. Cancer Clinical Trials* (in press).

COOKE, B. C., FIELDEN, E. M., JOHNSON, M. and SMITHEN, C. E., 1976. Polyfunctional radiosensitizers. 1. Effects of a nitroxyl biradical on the survival of mammalian cells *in vitro*. *Radiation Research*, *65*, 152–162.

DENEKAMP, J. and HARRIS, S. R., 1975. Tests of two electron affinic radiosensitizers *in vivo* using regrowth of an experimental carcinoma. *Radiation Research*, *61*, 191–200.

DISCHE, S., SAUNDERS, M. I., LEE, M. E., ADAMS, G. E. and FLOCKHART, I. R., 1977. Clinical testing of the radiosensitizer Ro.07.0582; experiences with multiple dose. *British Journal of Cancer*, *35*, 567–579.

GELEHRTER, T. D. Adrenal steroids, membranes and neoplasia. In *Current Topics in Molecular Biology*, Vol. 4. *Steroid Hormone Action and Cancer*. Ed. K. M. J. Menon and J. R. Reel (Plenum, New York), pp. 133–138.

HALL, E. J. and ROIZIN-TOWLE, L., 1975. Hypoxic sensitizers; Radiobiological studies at the cellular level. *Radiology*, *117*, 453–457.

JENTZCH, K., KARCHER, K. H., KOGELNIK, H. D., MAIDA, E., MAMMOLI, B., WESSLEY, P., ZAUNBAUER, F. and NITSCHER, V., 1977. Initial clinical experience with the radiosensitizing nitroimidazole Ro.07.0582. *Strahlentherapie*, *153*, 825–832.

KENNEY, F. T., 1962. Induction of tyrosine-α-ketoglutarate transaminase in rat liver. III. Immunochemical analysis. *Journal of Biological Chemistry*, *237*, 1610–1614.

MARTINDALE, 1976. Dexamethasone. *The Extra Pharmacopœia*. Ed. A. Wade (Pharmaceutical Press, London), p. 412.

MILLAR, B. C., FIELDEN, E. M. and MILLAR, J. L., 1978. Interpretation of survival curve data for Chinese hamster cells, V–79, using the multitarget, multitarget with initial slope and α β equation. *International Journal of Radiation Biology*, *33*, 599–603.

REDWOOD, W. R. and COLVIN, M., 1980. Transport of melphalan by sensitive and resistant L1210 cells. *Cancer Research*, *40*, 1144–1149.

ROSE, C. M., MILLAR, J. L., PEACOCK, J. H., PHELPS, T. A. and STEPHENS, T., 1981. Differential enhancement of melphalan cytotoxicity in tumour and normal tissue by misonidazole. *Conference on Combined Modality Cancer Treatment: Radiation Sensitizers and Protectors. Cancer Clinical Trials* (in press).

STRATFORD, I. J., ADAMS, G. E., HORSMAN, M. R., KANDAIYA, S., RAJARATNAM, S., SMITH, E. and WILLIAMSON, C., 1980. The interaction of misonidazole with radiation, chemotherapeutic agents or heat: a preliminary report. *Cancer Clinical Trials*, *3*, 231–236.

THOMPSON, E. B., 1976. The cellular action of glucocorticoids in relation to human neoplasma. In *Current Topics in Molecular Endocrinology*, Vol. 4. *Steroid Hormone Action and Cancer*, pp. 114–138.

URTASUN, R. C., BAND, P. R., CHAPMAN, J. S., RABIN, H., WILSON, A. F. and FRYER, G. G., 1977. Clinical phase I study of the hypoxic cell radiosensitizer Ro.07.0582, a 2-nitroimidazole derivative. *Radiology*, *122*, 801–804.

WASSERMAN, T. H., PHILLIPS, T. L., VAN RAALTE, G., URTASUN, R. C., PARTINGTON, J., KOZIOL, D., SCHWADE, J. G., GANGJI, D. and STRONG, J. M., 1980. The neurotoxicity of misonidazole; potential modifying role of phenyl in sodium and dexamethasone. *British Journal of Radiology*, *53*, 172–173.

WORKMAN, P., 1980. The neurotoxicity of misonidazole: potential modifying role of dexamethasone. *British Journal of Radiology*, *53*, 736.

1981, *British Journal of Radiology*, 54, 512–516

Technical note

A communication system for the transmission of nuclear medicine images over standard telephone lines

By J. R. Corfield, B.Sc., M.Sc., C. P. Wells, B.Sc., M.Sc. and F. M. Hall, M.B, Ch.B, D.M.R.T.

Kent and Canterbury Hospital, Canterbury

P. Vernon, B.Sc., M.Sc.

New Charing Cross Hospital, London

and D. N. Croft, M.A., D.M., F.R.C.P.

St. Thomas's Hospital, London

(Received October 1980 and in revised form January 1981)

With the development of nuclear medicine the time is approaching when small departments are likely to be established in many hospitals. However, due to financial constraints these small units will not be served by full-time, trained consultants in the specialty nor will they be equipped with full computer facilities for processing image data.

A practical solution is that central departments of nuclear medicine should be linked to the peripheral departments, allowing full data processing to take place in the main department together with clinical interpretation. This would be followed by rapid transmission of the report back to the peripheral centre.

There is a parallel problem in that there is no agreed standard format to present the results of nuclear medicine imaging. In consequence a clinician serving several centres could be faced with interpreting data in a variety of formats. This variety of format also makes for considerable difficulty in comparing results from different centres. A solution to this problem would be to obtain the image data in their basic form and to display them in the local display format. This again requires some form of data transmission between nuclear medicine centres.

Such a scheme has been implemented between a number of centres (Daly *et al.*, 1975). This involved the establishment of a main computer linked via leased telephone lines to satellite computer systems located in peripheral centres. It was based on a single manufacturer's equipment and through the use of expensive leased lines was in effect a hard-wired system only available to departments directly connected.

Another approach using a video signal converter to send images over standard telephone lines has been reported (Maxfield *et al.*, 1975). The output of a video camera viewing an image is converted for transmission over the telephone line. When the signals are received they are converted for display on a video monitor. This system has the disadvantages that the data are degraded during transmission to such an extent that data processing at the receiving end is not possible.

We have implemented a simple system combining the data processing capability of the computer-based approach together with the flexibility of using the public switched telephone network. In this paper we report the work of the pilot study undertaken to assess the problems involved.

REQUIREMENTS OF THE SYSTEM

Communication links

The main problem with long-distance communication links is that errors can occur in the data being transferred due to noise on the line. It is necessary therefore to adopt strategies which minimize the effect of such errors and to detect them wherever possible. The effect of errors can be minimized by sending the data in a rigid structured form and using error detection routines to recognize bad data. Rather than check every bit of data for error it is faster to send data in pre-defined blocks which can be retransmitted if the receiver recognizes an error. This approach involves defining a complete command and data protocol.

Choice of system

Having decided upon a digital communication link there are two basic methods of achieving it. The most common method of direct communication between computers over long distances is to use synchronous transmission over leased lines. This approach gives the highest speeds of transmission but at the expense of costly leased lines, sophisticated communication hardware and complex software to provide an extremely high level of error rejection.

The alternative approach is that used for linking remote terminals to computers and involves asynchronous data transmission. This approach is less efficient and therefore slower. However, it requires much less expensive hardware and simpler software and can use the public switched telephone network on a dial-up basis. It therefore avoids the high cost of renting a dedicated telephone line and can use the whole telephone network. However, there is normally minimal error checking associated with this method. With sophisticated hardware it is possible to achieve moderately high data rates of up to 240 characters per second.

Our initial requirement was to establish a link between two dissimilar computers located at Canterbury and London. As a pilot study we required the hardware to be inexpensive and the software to be easily developed for each computer system. The enormous rental of a leased line determined that the public switched telephone network should be used. It was therefore decided to investigate the asynchronous transmission approach and to incorporate error rejection techniques akin to those used in synchronous transmission protocols.

METHOD

The communication system implemented requires a small computer interfaced to a modem (to connect to the public telephone network) to be at either end of the link. In this system the computer is that in a nuclear medicine image processing system and the modem is an acoustic coupler connected by a serial line interface to the computer and a telephone handset. The serial line interface converts the data to and from the computer to and from a sequence of zeroes and ones. The acoustic coupler converts the zeroes and ones to and from pure tones transmitted over the public telephone network. A special program held in each computer enables one or more frames of data to be transmitted in either direction.

Protocol

On establishing the link, one end of the line is defined as the Master and the other as the Slave. The Master initiates the transmission of data.

A synchronization routine is required at the start of transmission. For this the Master issues a synchronization code and awaits a reply. This is repeated until five consecutive "acknowledge" replies have been received. The Master then issues its first command and the transmission can commence.

The basic sequence of events involved in transmitting an image is given in Table I. The first column indicates the type of information issued by the Master and the second column gives the command words or the data actually transmitted.

If the Slave fails to recognize a command or detects an error in the data block it replies with a "not acknowledge" and the Master retransmits the characters as detailed in Table II.

A command consists of two characters. A data block consists of 64 characters and 2 check sum characters for error checking. An "acknowledge" and a "not acknowledge" consist of 2 characters plus a third character called a switch character by which the Slave can communicate with the Master. This switch character is currently only used to change the roles of Master and Slave.

All characters consist of 8-bit binary words. This enables data in the range 0 to 255 to be transmitted. In this pilot study the image data consist of a 64 × 64 element array of display points and the data are transmitted one line per block. This use of a fixed

TABLE I

STANDARD TRANSMISSION SEQUENCE

	Master	Slave
Command	"Synchronize"	Acknowledge
Command	"Synchronize"	Acknowledge
	⋮	⋮
	After 5 successive acknowledges	
Command	"Start of text"	Acknowledge
Command	"Message"	Acknowledge
Data block	Message text block	Acknowledge
Command	"End of text"	Acknowledge
Command	"Start of text"	Acknowledge
Command	"Data block A"	Acknowledge
Data block	Identification block	Acknowledge
Command	"Data block B"	Acknowledge
Data block	1st line of image	Acknowledge
Command	"Data block A"	Acknowledge
Data block	2nd line of image	Acknowledge
	⋮	⋮
Command	"Data block B"	Acknowledge
Data block	Last line of image	Acknowledge
Command	"End of text"	Acknowledge
	⋮	⋮
Command	"End of transmission"	Acknowledge

TABLE II

Command word character values (in base 10)

Command word	First character	Second character
"Acknowledge"	113	199
"Not Acknowledge"	142	56
"Synchronize"	170	170
"Message"	136	136
"Data block A"	68	68
"Data block B"	34	34
"Start of text"	153	153
"End of text"	17	17
"End of transmission"	102	102

TABLE III

Fixed format identification block

Character numbers	Information
1–18	Patient's name
19–24	Date of investigation
25–36	Identification number
37–42	View (coded)
43–44	View number in sequence
45–46	Total number of views in sequence
47	Scaling factor (binary)

length block does not prevent the transmission of other image sizes.

Error rejection

As indicated earlier, error rejection is usefully achieved by formatting the data in such a way that the receiver knows what to expect at all times. In practice this means that the data are in fixed blocks, specified by the previous information. In our protocol, the first information to be sent is always a command and this has always to be acknowledged.

Since in practice there need only be a few commands, their binary patterns of zeroes and ones are made as different from each other as possible, so that the occurrence of noise is least likely to cause the command to be incorrectly recognized. This is achieved by comparing the received pattern with each command pattern in turn and measuring the closeness of fit. If the fit is good the command is recognized and the Slave replies with an "acknowledge". If the fit is poor than a "not acknowledge" is issued.

Since the Slave has only to reply with "acknowledge" or "not acknowledge", these codes are made so different that noise cannot cause them to be mistaken for each other.

This approach relies on redundancy in the data transmitted and this can be improved by increasing the number of bits used. Thus 16 bits rather than just 8 bits are used for command words.

The image data are sent in a fixed format block of 64 characters plus 2 sum check characters. These latter 2 are the summation of all the data in the preceding 64 characters. If errors have occurred in the data the sum check should detect them. If the block is made too long, multiple errors may occur which may still give the correct sum check. The length of the block should therefore be short enough so that only a few errors will occur in it. The block length of 64 characters was based upon the figures for error rates published by the United Kingdom Post Office (*Handbook of Data Communications*, 1975) which suggested an error rate of approximately 1 in 10^3 bits. It was originally intended to implement a more sophisticated method of block error checking called cyclical redundancy but the results with the sum check showed this to be unnecessary.

Also included in the protocol are timing checks. These are required to detect a failure of the line both partially and totally.

Image identification

To make for an interactive system the protocol includes the ability to send messages between the Master and Slave. These are free format and are directed to the operator's console. They provide user to user transfer of information other than via voice contact over the telephone line and can be used to indicate the type and amount of data to be transmitted.

Each image transmitted must be properly identified. The first block associated with each image is a fixed format identification block. A format similar to that suggested by Brown (1975) has been implemented and is shown in Table III. These identification data and also the message block are coded as ASCII data.

Image data coding

To maximize the transmission speed it was deemed acceptable to scale all image data to a working maximum value of 255 by division of a power of 2. This power factor is contained in the identification block. Thus each image point, suitably scaled, is transmitted as a single character.

Software implementation

The program to implement the link is written as a set of subroutines in the high-level language Fortran IV. In addition some machine code routines to handle the serial line interface are required.

The data to be transmitted and received are held as Fortran files from which they may be converted to the local image-data storage format using, as appropriate, information held in the identification block.

RESULTS

The system has been installed in three centres: The Kent and Canterbury Hospital, St. Thomas' Hospital and Charing Cross Hospital. The program has been shown to be straightforward to implement on two dissimilar machines: a Digital Equipment PDP8E at Canterbury and a Varian Associates Varicam at London.

In this pilot scheme only acoustic couplers working at 300 baud have been used and an image of 64×64 elements can be transmitted in approximately three minutes. The exact time depends upon the number of retransmissions required due to noise.

The error rate over the public switched telephone network between Canterbury and London has been measured and a typical result gave 405 bits in error out of 57000 words transmitted. These measurements confirm the bit error rate to be approximately one in a thousand, as expected.

To test the system several hundred test images have been transmitted and no errors have been found to get through to the final received image. The error rejection techniques employed have been found to be adequate and the system is found to operate in a logical way under a variety of conditions. If, for example, the telephone connection is broken during image transmission, the programs in each centre try the line several times, but if no response is received a message is displayed at the terminals and the program then allows telephone contact to be re-established before restoring communications.

DISCUSSION

The original concept for this study was to see if it would be feasible to connect small nuclear medicine centres to a central department. With the availability of small data acquisition units such an arrangement could be satisfactory provided a communication system could be easily established. The system developed would seem to fill this role with few constraints on the type of acquisition unit used in each centre.

Apart from the serial line interface (typically £300–£600) which many systems will already have, the only other hardware cost is that of the connection to the telephone system; in the work described here an acoustic coupler costing under £200 was used.

The type of image transmitted using the system is not limited to nuclear medicine images. All images which are stored as a digital matrix, including computed tomography and ultrasound data, could be transmitted. Although the current matrix is 64×64 elements this is only for convenience and to reduce transmission times during the pilot study.

Clearly for intensive usage and larger image matrices, higher transmission rates are required. With a relatively modest increase in hardware costs the baud rate could be raised to 2400 bits per second, which would result in an eight-fold reduction of transmission time to approximately 20 s per image.

Almost by definition, each element in an image is related in amplitude to those adjacent to it and there is thus much redundancy in the data. Many and various sophisticated techniques have been published (Tescher, 1976) to reduce such data to the minimum necessary to transmit the actual information present. As an example, a simple data reduction technique would be to transmit only the differences between adjacent picture points.

For many nuclear medicine images the image is roughly a circle inscribed inside the matrix, leaving many elements unused. It is clearly wasteful to send data for these points.

By such data reduction techniques a further factor of 2 or 3 could be achieved in transmission speeds, albeit at the expense of increased processing time before and after transmission.

As well as providing the link between peripheral and central nuclear medicine centres, the system provides a standard format in which to exchange data. In 1975 the Nuclear Medicine Computer Users' Group promoted a standard image-data format which has been successfully used to exchange data between many centres on paper and magnetic tape. However, there are centres which do not have facilities to read either magnetic or paper tape and the communication system described here provides a potentially more widely available format.

These exchanges could be used to create large data pools from several centres to enable diagnostic criteria for new imaging techniques to be more rapidly established. Also, the interchange of test images could be undertaken to allow comparison of the data-processing techniques used in different centres with identical image data.

Conclusions

The system developed is easy and inexpensive to implement on most nuclear medicine computer systems. Moderate transmission speeds are obtained and error checking has been found to be adequate to remove all errors in the images transmitted to date.

We would welcome collaboration with other centres to establish the communication link and assess the ease of implementation on other systems.

Acknowledgment

This work was supported by a grant (LORS 76/54) from the South East Thames Regional Health Authority.

REFERENCES

Brown, N., 1975. Private communication via the Nuclear Medicine Computer Users' Group Newsletter No. 5.

Daly, J. L., Herbig, K. F. and Fletcher, J. W., 1975. A nuclear medicine information network. *Journal of Nuclear Medicine, 16*, 523

Maxfield, W. S., Miale, A. and Krauss, J. S., 1975. Consultation via telephone transmission of scans. *Journal of Nuclear Medicine, 16* ,549

Tescher, A. G. (Editor), 1976. Advances in image transmission techniques. *Proceedings of the Society of Photo-optical Instrumentation Engineers, 87*, August 1976.

The UK Post Office, 1975. *Handbook of Data Communications* (NCC Publications), p. 180.

Book reviews

Radiation Drug Interactions in the Treatment of Cancer. By G. H. Sokol and R. P. Maickel, pp. xvi+235, 1980 (John Wiley, Chichester/New York), £16·00.
ISBN 0-471-04697-3

Although there are 14 contributors to this book it is well edited to present a coherent theme starting with the physics of radiotherapy, through protection, basic radiobiology into pharmacology and chemotherapy. En route the subjects of hypoxia, sensitizations and radioprotective agents are covered. Much of the evidence considered derives from clinically orientated animal experiments. This has resulted in a rather optimistic and apparently tidy presentation which tends to leave the reader wondering why cure rates are still so poor in some cases.

On a more positive side, a useful description of the basic pharmacology relating to cancer chemotherapy is given in Chapter 3. Interactions between drugs and the body, involving absorption, distribution, and metabolism phenomena and excretion processes, are clearly presented and related to pharmacodynamic considerations. The importance of such concepts when chemotherapy is being considered in the treatment of cancer is stressed.

The section on the clinical pharmacology of anticancer drugs (Chapter 4) deals with the main groups of different types of cancer chemotherapy agents, with specific reference to those most commonly encountered in clinical practice. Although the description of each group is necessarily brief, the chemical structures and pathways of metabolic activation and deactivation are well presented and clear.

This book appears to be aimed at the F.R.C.R. student and beyond, and this aim is well justified. In addition it can be recommended for general clinicians' reading.

A. W. Preece,
P. Ann Light.

Topical Reviews in Radiotherapy and Oncology. Vol. 1. Ed. Thomas J. Deeley. pp. viii+274, 1980 (John Wright, Bristol), £13·50
ISBN 0-7236-0538-6

This is an informative book consisting of ten chapters on various aspects of radiotherapy and oncology. As Dr. Deeley himself points out these are highly selected and much of equal interest is omitted. There are only three anatomical sites discussed, the breast, brain and oesophagus, and three other chapters are devoted to general topics of cancer information and a general review of radiotherapy and oncology. Immunology and hypoxic cell sensitizers in malignant disease each have a chapter and there is a detailed assessment of some of the factors concerned in accuracy in radiotherapy, which provokes thought and calls for action to reduce errors.

Some of the figures on the diagrams are difficult to read and there are printing errors which now seem to be standard practice in new publications.

This book provides easy reading on interesting subjects and will appeal to many of those who are concerned in the broadest sense with oncology.

Mary Catterall.

1981, *British Journal of Radiology*, *54*, 517–518 JUNE 1981

Case reports

Léri's pleonosteosis

By M. Friedman, F.R.C.P.,

London,

B. M. Lawrence, F.R.C.P. and D. G. Shaw, F.R.C.R.

Queen Elizabeth Hospital for Children, London E2

(*Received November 1980*)

Radiological bone age is usually requested for any child who is short. Two such requests led to the recognition of digital changes characteristic of Léri's pleonosteosis.

CASE REPORTS

Case 1, a male, was born five weeks prematurely, weight 2.55 kg. After some initial respiratory distress progress was satisfactory. His parents were Danish. At three years 11 months, he was seen because of short stature, with a height below the third percentile. Physical examination revealed rather short stubby hands, feet and limbs. Biochemical investigations included tests for urinary mucopolysaccharides and amino acids, thyroid and renal function and calcium metabolism. All were normal. The bone age was retarded. Over the next three years, no biochemical or other abnormalities were discovered but there was progressive broadening and stubbiness of the fingers with progressive flexion deformity and limitation of flexion and extension. A radiograph of the hands showed marked broadening of the phalanges which were short and held in flexion. (Fig. 1). A skeletal survey revealed ischaemic necrosis of both femoral heads but no other abnormality. At a chronological age of 6.5 years, the bone age was 3.5 years and his stature was 9 cm below the third percentile. Clinically the face was rather flat.

Case 2, a Greek boy, was perfectly well until the age of 3.5 years when he presented with difficulty in opening and closing his hands. This stiffness gradually spread to involve his elbows, shoulder joints, feet and ankles and then the knees. There was no pain and the child was otherwise well. On examination at seven years of age, the significant findings were claw-like deformity of both hands with slight flexion deformities of both elbows and limitation of shoulder movement. Biochemical investigations were normal and electromyography unremarkable. Radiographs of the hands and feet (Figs. 2 and 3) showed a characteristic widening of the phalanges with evident mild flexion deformity.

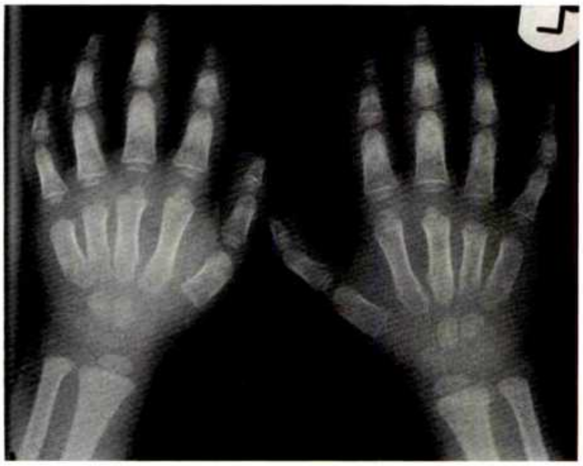


FIG. 1. *Case 1*.
Broad phalanges and flexion deformity of fingers.

DISCUSSION

The clinical and radiological features noted in the hands of these children are characteristic of Léri's pleonosteosis. Léri (1921) described a kindred characterized by broadening and deformity of the thumbs, flexion contractures of the fingers and of the toes, limited movements of other joints, shortness of stature and, often, rather flat mongoloid faces.

The earlier French literature is considerably more expansive than the English although Watson-Jones (1959) described carpal tunnel compression and Morton's metatarsalgia in association with Léri's pleonosteosis. The condition is inherited as an autosomal dominant with good penetrance and a variable expression. The radiological manifestations are most prominent in the hands and feet although increase in the width of the vertebrae and bizarre enlargement of the posterior neural arches of the cervical vertebrae are reported (Rukavina *et al.*, 1959).

Awareness of this condition is of some practical importançe as these children may at first be diagnosed as a collagenosis, rheumatoid disease, mucopolysaccharidosis or mucolipidosis. The aetiology is unknown although Watson-Jones suggested the primary pathology may be in the joint capsules rather than in the bone itself. The significance of the ischaemic necrosis of the femoral capital epiphyses in Case 1 is uncertain. Although Rocher and Roudil (1932) described advanced maturation of the femora in early childhood, an increase in size of the femoral capital epiphyses with coxa vara has also been noted. The reasonable height of Case 2 is a reflection of the variable expression of the condition. Although these two children were of continental extraction, it seems

1981, *British Journal of Radiology*, *54*, 518–521

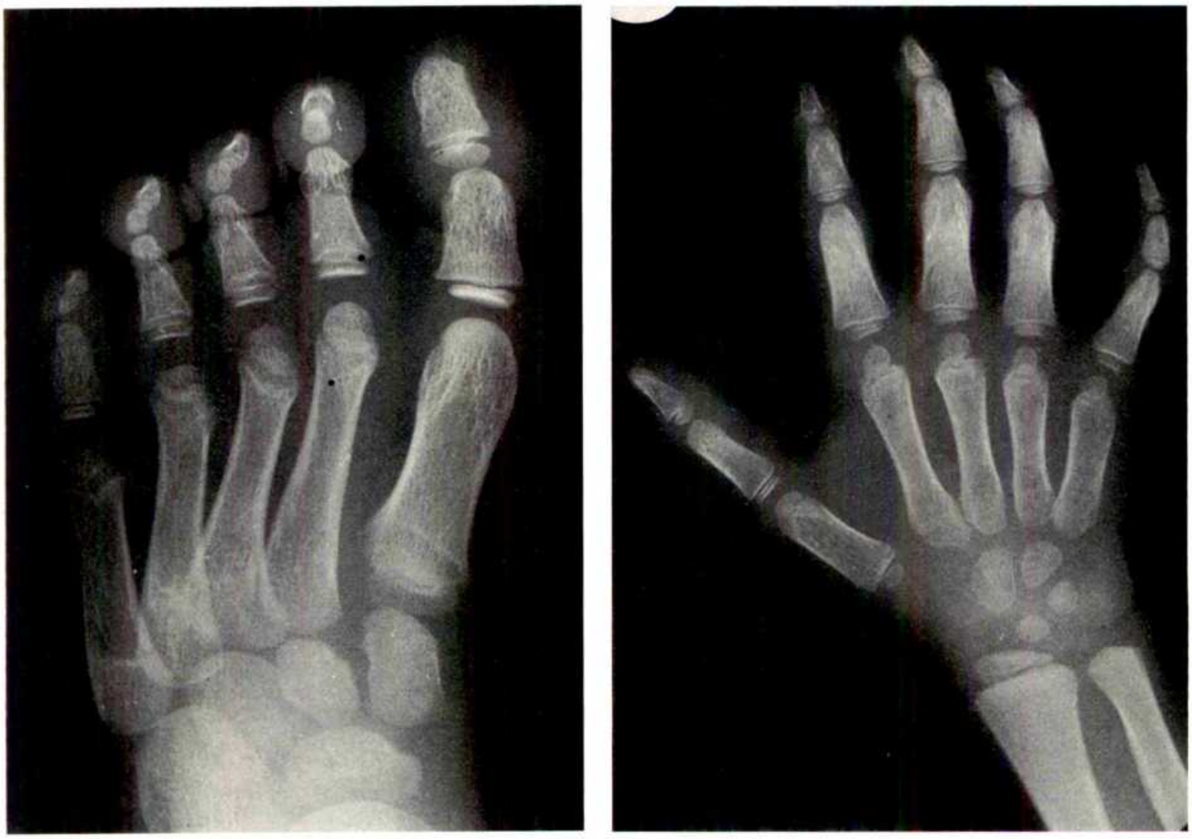


FIG. 2. FIGS. 2 and 3. *Case 2.* FIG. 3.

Broad phalanges and flexion deformity.

likely that the condition may be more frequent than the literature in this country suggests.

REFERENCES

LÉRI, A., 1921. Une maladie congénitale et héréditaire de l'ossification: la pléonostéose familiale. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, *45*, 1228.

ROCHER, H. L. and ROUDIL, G., 1932. La pléonostéose (maladie de Léri). Etude anatomo-clinique et radiographique, *Bordeaux chirurgical*, *4*, 359.

RUKAVINA, J. G., FALL, H. F., HOLT, J. F. and BLOCK, W. D., 1959. Léri's pleonosteosis. A study of a family with a review of the literature. *Journal of Bone and Joint Surgery*, *41-a*, 397.

WATSON-JONES, R., 1959. Léri's pleonosteosis. Carpal tunnel compression of the median nerves and Morton's metatarsalgia. *Journal of Bone and Joint Surgery*, *31-b*, 560.

Histoplasma duboisii infection of bone

By *E. M. Thompson, M.A., M.R.C.P., †J. Ellert, M.B., Ch.B., ‡L. L. W. Peters, F.R.C.S.

Departments of *Pathology and †Radiology, Northwick Park Hospital, and ‡The Westfield Clinic, Banjul

A. Ajdukiewicz, B.Sc., M.B., Ch.B., M.R.C.P. and D. Mabey, B.M., B.Ch., M.R.C.P.

MRC Unit, Banjul, The Gambia

(*Received November 1980*)

Histoplasma duboisii infection not uncommonly affects bones. When this is associated with overt infection elsewhere recognition is relatively easy. However, when bony involvement is the primary manifestation, the clinical and radiological changes may closely simulate a malignant neoplasm and provide diagnostic difficulty. We report such a case with a solitary lesion of the femur.

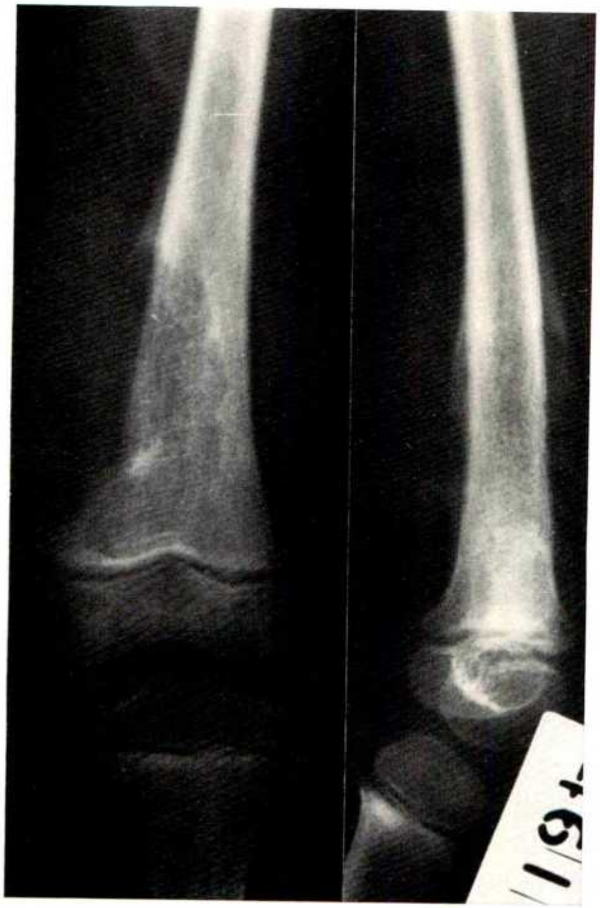
CASE REPORT

A thin four-year-old Gambian girl presented with a two months' history of low grade pyrexia and a painful swelling of two weeks' duration at the lower end of the left thigh. There was no significant previous medical or family history.

On examination she had a tender egg-shaped tumour at the lower end of the left femur with bilateral shotty inguinal lymphadenopathy. There was no hepatosplenomegaly or other obvious skeletal disease and there were no cutaneous lesions.

Radiography showed a large destructive lesion at the lower end of the femur extending to the metaphyseal line (Fig 1A, B). There was periosteal elevation proximally with formation of a Codman's triangle. Surrounding soft tissue swelling was marked. The radiological findings were initially thought to be in keeping with a malignant bone tumour. However, on close inspection there is faintly scalloped margination of the supero-lateral border of the lesion with a narrow band of transition which is more consistent with an infective process.

Histological sections from the lesion showed granulomatous inflammation which was destroying bone. It was characterized by many giant cells. Numerous yeast-like fungi up to 20 μm in diameter were seen both intra- and extracellularly. These contained a single nucleus and capsular stains were negative. No calcification was present. These features are characteristic of *H. duboisii* infection.


A FIG. 1. B

AP and lateral views showing a large destructive lesion at the lower end of the left femur extending to the metaphyseal line. There is periosteal elevation proximally with formation of a Codman's triangle and marked surrounding soft tissue swelling. The superolateral border of the lesion shows faintly scalloped margination with a narrow zone of transition.

Treatment and progress

Following bone biopsy she developed a sinus at the site of operation. Disseminated skin lesions of histoplasmosis occurred about four weeks later. Lymphadenopathy was noted in the neck, axillae and groins (Fig. 2A, B).

Amphotericin B was given intravenously in gradually increasing doses starting at 3 mg and increasing to 16 mg daily. The total dose was 293 mg. There were no reactions except with the last dose of Amphotericin B when fever and vomiting occurred. The swelling at the lower end of the femur gradually resolved and was almost healed two months after the start of therapy. She felt better in herself and gained 1·6 kg in weight.

DISCUSSION

Reports of *H. duboisii* infection have been confined to Africa between the Sahara and the Kalahari deserts. This distribution contrasts with *H. capsulatum* which has a worldwide distribution and is a distinct entity clinically and pathologically (Lunn, 1960) affecting bones very rarely (Klingberg, 1950; Allen, 1959; Key and Large, 1942; Schwartz, 1962). The commonest site for a primary lesion in *H. duboisii* infection is the skin. Disseminated lesions may occur in many organs and skeletal manifestations occur in up to two thirds of cases (Cockshott and Lucas, 1964a). Williams *et al.* (1971) reported the femur to be the most frequently affected bony site. The focus in long bones of young children tends to be diaphyseal whereas older children and adults show juxtametaphyseal involvement, a fact possibly related to the regression of marrow towards the metaphysis with increasing age.

The pathological process begins in the medulla, destroying adjacent bone trabeculae and eroding cortical bone from within (Cockshott and Lucas, 1964b). This may be accompanied by periosteal reaction and reactive new bone formation (Murray and Jacobson, 1977). The granulomatous lesion may extend further into soft tissue with the development of a cold abscess which usually ruptures with sinus formation.

Radiographically skeletal lesions appear as irregular, usually multiple, areas of bone destruction (Murray and Jacobson, 1977). Drexler (1968) described three types of destructive bone lesion demonstrating marginal osteolysis, central osteolysis or massive bone destruction with abscess formation. Healing when it occurs begins peripherally. The radiological appearances of *H. duboisii* infection are not pathognomonic and the differential diagnosis should include primary and secondary malignancies of bone as well as other infections.

The radiological differentiation from a malignant tumour may be extremely difficult. In this case the most likely diagnosis was felt to be an osteosarcoma despite the age of the patient and the absence of any associated sclerosis. The usual age range for osteosarcoma is from ten to 25 years, and the presence of dense irregular sclerosis is a usual feature of associated new bone formation. Other malignant bone tumours which might also be considered are a solitary neuroblastoma and a Ewing's tumour. However, less than 5% of Ewing's tumours present under the age of five. They also tend to have a predilection for the metaphysis in long bones and usually present as a mottled infiltrative destructive lesion with a wide zone of transition.

Pyogenic osteomyelitis and tuberculosis may both present as a solitary destructive lesion of bone with a periosteal reaction. In the early stages of pyogenic osteomyelitis with minimal or no sclerosis, the lesion may appear to be essentially osteolytic with a soft tissue swelling obliterating the intervening soft tissue planes. However, this is usually followed by the development of bony sequestra. Tuberculosis normally involves the metaphysis and periosteal reaction is not a prominent feature in this condition.

The natural history of *H. duboisii* is to run a chronic course with phases of regression and progression with a strong tendency to spontaneous healing. Before epiphyseal fusion has occurred, a lesion close to the metaphysis may cause disturbance

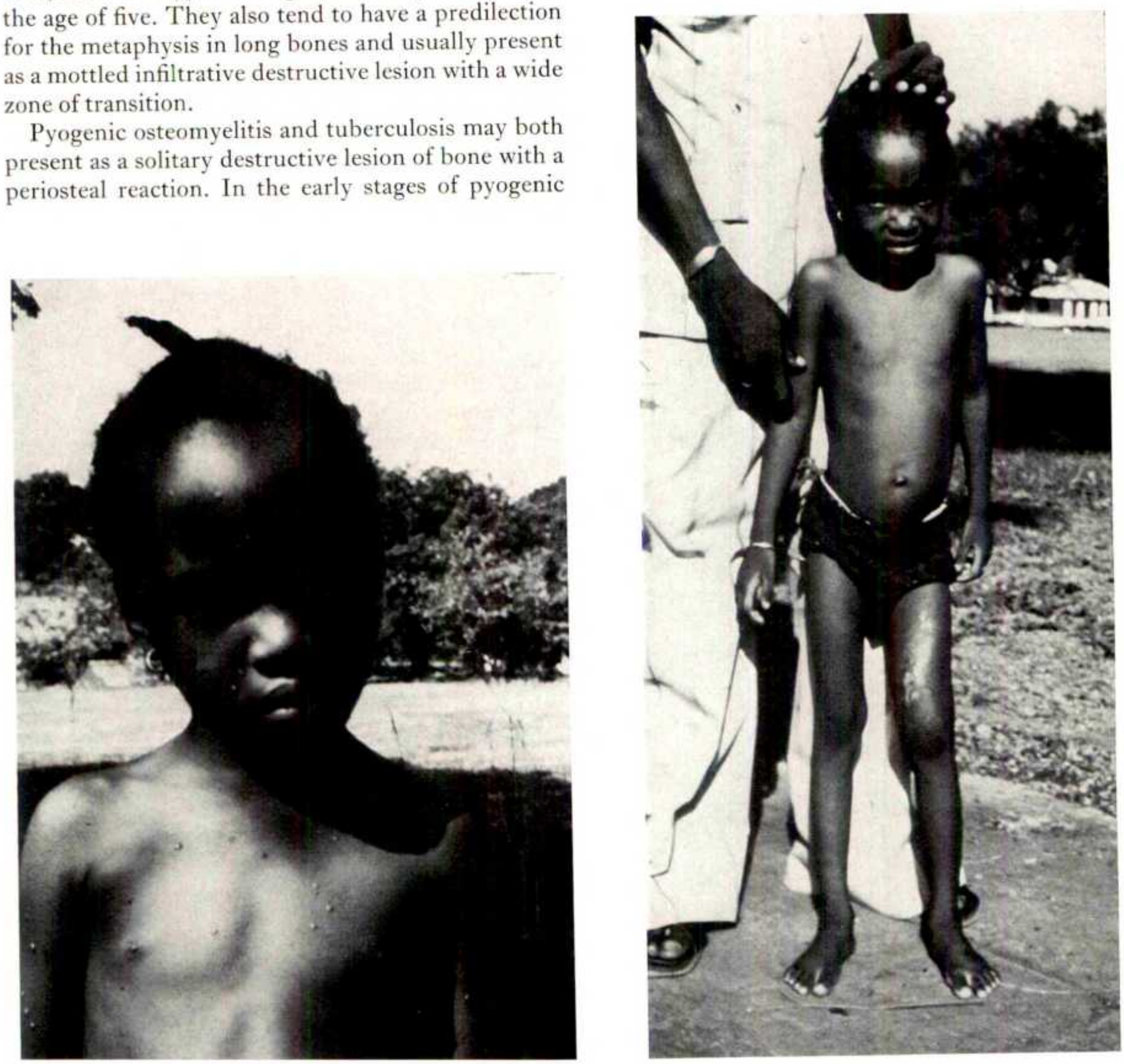

A B

FIG. 2.

The patient just before the start of treatment. (A) Wide-spread skin nodules of *H. duboisii*. (B) The discharging sinus above the left knee at the site of bone biopsy.

of epiphyseal growth with permanent deformity despite subsequent healing. This may be of future relevance in this young patient.

In conclusion it should be stressed that *H. duboisii* presenting as a solitary bone lesion may be very difficult to differentiate from a malignant bone tumour radiologically, but when it is suspected a skeletal survey should always be done to exclude additional clinically silent foci of infection.

ACKNOWLEDGMENTS

We should like to thank Dr. Kreel and Dr. Slavin for their helpful suggestions; the Department of Medical Photography, Northwick Park Hospital, which produced the prints; and the technicians in the Histopathology Department who processed the biopsy material.

REFERENCES

ALLEN, J. H., 1959. Bone involvement with disseminated histoplasmosis. *American Journal of Roentgenology*, *82*, 250–254.

COCKSHOTT, W. P. and LUCAS, A. O., 1964a. Histoplasmosis duboisii. *Quarterly Journal of Medicine*, *33*, *130*, 223–238.

COCKSHOTT, W. P. and LUCAS, A. O., 1964b. Radiological findings in *Histoplasma duboisii* infections. *British Journal of Radiology*, *37*, 653–660.

DREXLER, L., 1968. The radiological aspects of African histoplasmosis. *Annales de la Société belge de médicine tropicale*, *48*, 607–612.

KEY, J. A. and LARGE, A. M., 1942. Histoplasmosis of knee. *Journal of Bone & Joint Surgery*, *24*, 281–290.

KLINGBERG, W. G., 1950. Generalized histoplasmosis in infants and children; review of ten cases, one with apparent recovery. *Journal of Pediatrics*, *36*, 728–741.

LUNN, H. F., 1960. A case of histoplasmosis of bone in East Africa. *Journal of Tropical Medicine and Hygiene*, *63*, 175–180.

MURRAY, R. O. and JACOBSON, H. G., 1977. *Radiology of Skeletal Disorders*. 2nd ed., vol. 1 (Churchill Livingstone, London/Edinburgh/New York), pp. 464, 618.

SCHWARTZ, E., 1962. Regional roentgenological manifestations of histoplasmosis. *American Journal of Roentgenology*, *87*, 865–874.

WILLIAMS, A. O., LAWSON, E. A. and LUCAS, A. O., 1971. African histoplasmosis due to *Histoplasma duboisii*. *Archives of Pathology*, *92*, 306–318.

Retropharyngeal bleeding in haemophilia

By R. I. Markowitz, M.D.

Department of Diagnostic Radiology, Yale University School of Medicine and the Yale-New Haven Hospital, New Haven, CT, USA

and J. B. Mendel, M.D.

Department of Radiology, Hospital of St. Raphael, New Haven, CT, USA

(Received October 1980 and in revised form January 1981)

The common bleeding sites in patients with haemophilia include the joints and peripheral soft tissues. Haemorrhage at these locations is usually not life-threatening but can result in acute and chronic disability. Bleeding within confined spaces such as the skull or spinal canal, or within large fascial planes such as the retroperitoneum, may be more critical and can result in death if not recognized and treated promptly. A less common but potentially fatal complication is upper airway obstruction and suffocation resulting from haemorrhage within the retropharyngeal and paratracheal soft tissues of the neck.

CASE REPORT

A 20-year-old white male was diagnosed as having classical haemophilia, type A, as an infant. In recent years, he had been seen numerous times in the emergency room for recurrent haemarthroses. Four days prior to admission, he developed a mild sore throat without cough or fever. Dysphagia became progressively worse and the evening prior to admission he claimed he was unable to eat or sleep for fear of his "throat shutting off". He denied any recent trauma, choking, upper respiratory infection, or excessive shouting.

Physical examination revealed a well young man in no distress. The vital signs were normal. Examination of his oropharynx revealed no evidence of bleeding from the gums or oral mucosa. The posterior pharyngeal wall was symmetrical without bulging or discoloration. Indirect laryngoscopy showed a normal epiglottis, tongue and hypopharynx. The patient's neck was supple, but there was tenderness to palpation over the sternocleidomastoid muscles as well as discomfort with side-to-side motion of the hyoid and trachea. The remainder of the physical examination was non-contributory.

Radiographs of the neck showed diffuse widening of the retropharyngeal soft tissues with anterior displacement of the trachea (Fig. 1). Fluoroscopy revealed that the deformity of the posterior pharyngeal wall was constant and fixed. A barium swallow demonstrated that the oesophagus was also displaced anteriorly by a smooth fusiform prevertebral mass (Fig. 2). A chest radiograph was normal. The diagnosis of a retropharyngeal haematoma was made on the basis of these findings and treatment with Factor VIII concentrate was begun and continued for nine days, maintaining the Factor VIII titre at approximately 50%. Repeat radiographic examination obtained ten days later when the patient was asymptomatic showed the upper airway to be normal (Fig. 3).

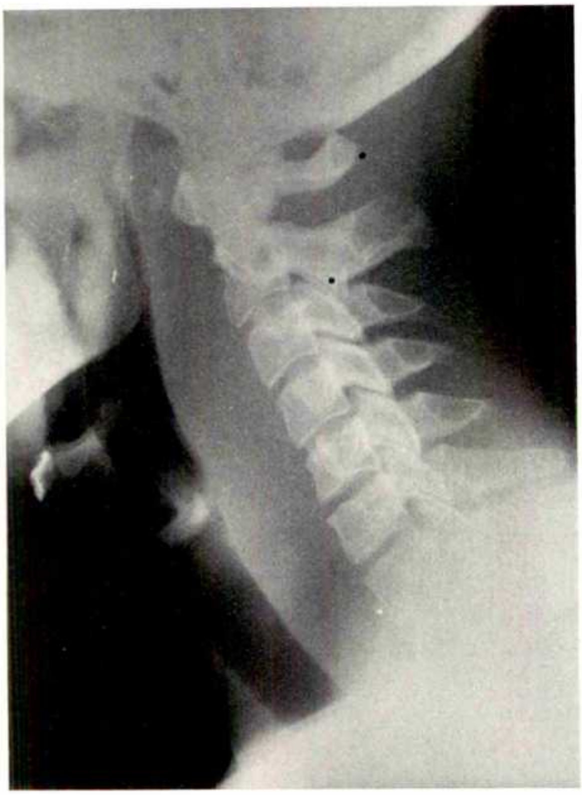


FIG. 1.

Lateral view of the neck during phonation shows fusiform widening of the retropharyngeal soft tissues with anterior displacement of the larynx and trachea.

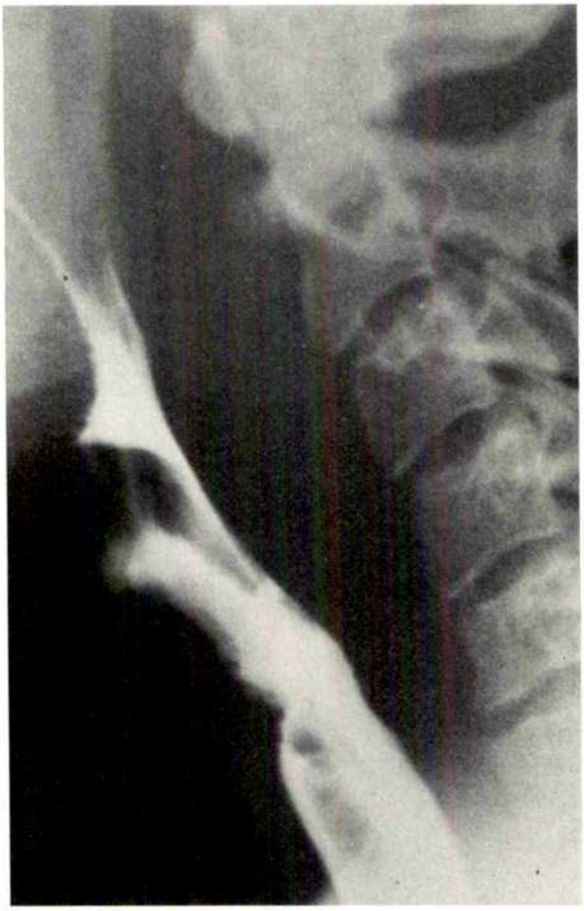


FIG. 2.

Spot film exposure from a barium swallow shows anterior displacement of the cervical oesophagus.

DISCUSSION

The major haemorrhagic complications of haemophilia involve bleeding within confined spaces, or sequestered blood loss within large fascial planes. Obstruction of the upper airway due to spontaneous bleeding is distinctly unusual, and in a recent review accounted for only one of 14 haemophilia related deaths (Lewis, 1970). Indeed, less than 40 cases of upper airway obstruction due to bleeding in haemophilia have been reported in the literature, only two of which were published in the last 12 years (Baird and Fox, 1943; Boyd, 1950; Colman, 1956; Davidson *et al.*, 1949; Edmonds, 1951; Endicott *et al.*, 1942; Fox *et al.*, 1946; Kitchens, 1977; Kiviranta, 1967; Leatherdale, 1960; MacDonald *et al.*, 1953; Pochedly and Rosales, 1968; Skolnik and Fornatto, 1955). There are no cases described in the radiology literature, although retropharyngeal bleeding secondary to trauma (Stein and Herschberg, 1970) or anticoagulant therapy (Owens *et al.*, 1975) is known.

Recognition of retropharyngeal bleeding may at first be difficult in that symptoms are often nonspecific and may mimic an upper respiratory infection. In our case, although the patient initially complained of a sore throat, he had no other symptoms of infection, thus demonstrating the point that "pharyngitis" may represent an early symptom of bleeding and not necessarily its cause (Baird, 1943; Boyd, 1950; Colman, 1956; Davidson *et al.*, 1949; Kitchens, 1977; Skolnik and Fornatto, 1955). In most cases retropharyngeal bleeding in haemophiliacs will be spontaneous (Leatherdale, 1960). As bleeding within the soft tissues progresses, swelling may become clinically apparent and eventually ecchymosis of the tissues may be observed (Pochedly and Rosales, 1968). It is important to recognize

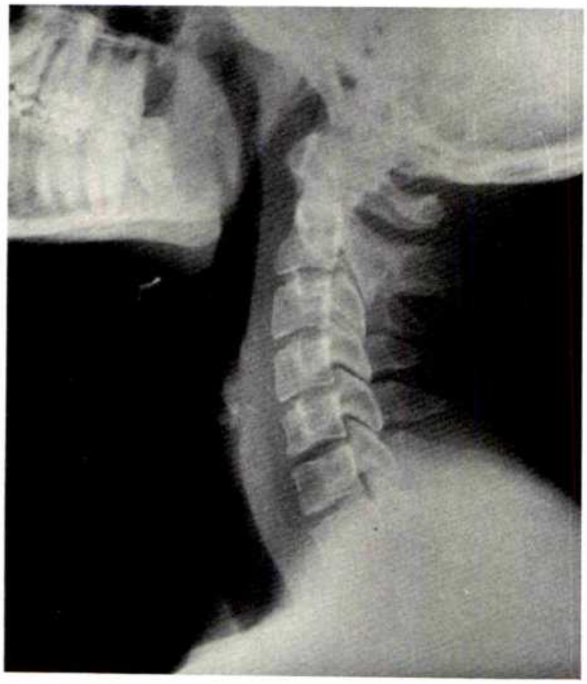


FIG. 3.

Follow-up lateral view of the neck shows a normal retropharyngeal space.

bleeding in and around the upper airway as early as possible in order to initiate replacement Factor VIII therapy and thus prevent complete airway obstruction and suffocation (Kitchens, 1977). Before the advent of Factor VIII replacement therapy, tracheotomy was often required and mortality was high (Baird and Fox, 1943; Kiviranta, 1967).

The radiographic appearance of the upper airway and retropharyngeal "space" in children and adults has been well described (McCook and Felman, 1979; Wholey *et al.*, 1958). Normal measurements have been provided by Wholey *et al.* who, on the basis of 600 normal lateral cervical radiographs, described as abnormal a retropharyngeal space (at C2) of greater than 7 mm and a retrotracheal space (at C6) of greater than 22 mm. In our case, the retropharyngeal space at C2 measured 20 mm with the widest distance of 23 mm occurring at C3–C5.

The diagnostic value of the radiographic examination in this particular clinical situation has not been adequately stressed. A diffuse swelling of the retropharyngeal soft tissue space may be hard to appreciate on physical examination because of the absence of a localized mass or bulge. Stein and Herschberg have reported a case of retropharyngeal bleeding in an adult following trauma to the occiput. The physical signs of a bulging posterior pharyngeal wall and ecchymosis were absent at a time when the radiographic examination showed extensive and diffuse widening of the retropharyngeal space (Stein and Herschberg, 1970). The case presented here similarly demonstrates the usefulness of the radiological evaluation in detecting an abnormality at a time when the clinical examination was normal.

ACKNOWLEDGMENTS

The authors thank Ms. Sandra Peffer for her help in the preparation of the manuscript.

REFERENCES

BAIRD, K. H. and FOX, M. S., 1943. Severe sublingual and paratracheal hemorrhage in hemophilia with recovery following tracheotomy. *Journal of Pediatrics*, *23*, 90–94.

BOYD, W. H. F., 1950. Respiratory obstruction in haemophilia. Recovery after intubation. *Lancet*, *i*, 302–303.

COLMAN, B. H., 1956. Haemophilia involving the pharynx and larynx. *Journal of Laryngology*, *70*, 540–543.

DAVIDSON, C. S., EPSTEIN, R. D., MILLER, G. F. and TAYLOR, F. H. L., 1949. Hemophila. A clinical study of forty patients. *Blood*, *4*, 97–119.

EDMONDS, A. R., 1951. Death from respiratory obstruction in haemophilia. *Medical Journal of Australia*, *1*, 227–228.

ENDICOTT, C. L., MITCHELL, J. H. and QVIST, G., 1942. Asphyxia following dental extraction in a haemophiliac (with a note on the spread of infection in Ludwig's angina). *British Medical Journal*, *ii*, 34–35.

FOX, J. R., SPENCER, J. T., Jr. and TOCANTINS, L. M., 1946. Dyspnea in hemophilia from hemorrhage into larynx. *Journal of the American Medical Association*, *130*, 78–80.

KITCHENS, C. S., 1977. Retropharyngeal hematoma in a hemophiliac. *Southern Medical Journal*, *70*, 1421–1422.

KIVIRANTA, U. K., 1967. Laryngeal haematomas due to coagulopathies. *Journal of Laryngology*, *81*, 503–513.

LEATHERDALE, R. A. L., 1960. Respiratory obstruction in haemophilic patients. *British Medical Journal*, *i*, 1316–1320.

LEWIS, J. H., 1970. Causes of death in hemophilia. *Journal of the American Medical Association*, *214*, 1707.

MCCOOK, T. A. and FELMAN, A. H., 1979. Retropharyngeal masses in infants and young children. *American Journal of Diseases of Children*, *133*, 41–43.

MACDONALD, A. C., ROBSON, J. G. and WAPSHAW, H., 1953. Haemophilia with respiratory obstruction. *British Medical Journal*, *i*, 1144–1146.

OWENS, D. E., CALCATERRA, T. C. and AARSTAD, R. A., 1975. Retropharyngeal hematoma. A complication of therapy with anticoagulants. *Archives of Otolaryngology*, *101*, 565–568.

POCHEDLY, C. and ROSALES, A., 1968. Respiratory obstruction in a child with classical hemophilia. *American Journal of Diseases of Children*, *116*, 103–105.

SKOLNIK, E. M. and FORNATTO, E. J., 1955. Management of respiratory obstruction in hemophilia. *Eye, Ear, Nose, Throat Monthly*, *34*, 435–438.

STEIN, H. and HERSCHBERG, S., 1970. Massive retropharyngeal hematoma: report of a case. *Journal of the American Osteopathic Association*, *70*, 260–262.

WHOLEY, M. H., BRUWER, A. J. and BAKER, H. L., JR., 1958. The lateral roentgenogram of the neck. *Radiology*, *71*, 350–356.

1981, *British Journal of Radiology*, 54, 524–526

Case reports

Renal opacification during intravenous urography in acute cortical necrosis (the nephrogram in cortical necrosis)

By N. B. Bowley

Department of Radiology, Hammersmith Hospital, London W1 20HS

(*Received August 1980 and in revised form January 1981*)

Acute renal cortical necrosis is a rare cause of acute renal failure. It can occur following a variety of insults but has been most commonly reported following obstetric complications (Kleinknecht *et al.*, 1973). The diagnosis is suspected when there is oliguria or anuria with little or no recovery within six weeks of onset in an appropriate clinical context. Confirmation of the diagnosis is usually made by renal biopsy but this may be unreliable if the necrosis is patchy (Wells *et al.*, 1960; Kleinknecht *et al.*, 1973). The radiographic demonstration of cortical "tramline" calcification has also been used to confirm a provisional diagnosis but only a minority of patients with cortical necrosis will develop this feature (Deutsch *et al.*, 1971; Kleinknecht *et al.*, 1973) and it is unusual to see such calcification until at least four weeks after the onset of necrosis.

It has been shown that distinctive appearances may be seen during renal arteriography and that these appearances may be used to confirm a diagnosis of acute cortical necrosis at an early stage (Deutsch *et al.*, 1971; Kleinknecht *et al.*, 1973). It is usually thought that opacification of the renal substance during intravenous urography does not occur in patients with acute cortical necrosis. However, three cases showing such opacification have been reported in the French literature (Joffre *et al.*, 1976) and the following case report is a further example. In all four cases the pattern of opacification was characteristic.

CASE REPORT

A 30-year-old woman presented with oliguric renal failure after a spontaneous abortion in the mid trimester of her second pregnancy. On admission she was normally hydrated but hypertensive (BP 200/100 mmHg). Urine volume was initially 450 ml/24 h but subsequently fell to 295 ml/24 h; there was no active urine sediment. Laboratory results were Hb 10.8 g/dl, anisocytosis, plasma creatinine 527 μmol/l (rising to 1370 μmol/l), blood urea 25 mmol/l, serum albumin 24 g/l, urinary protein excretion 0.3 g. She was commenced on peritoneal dialysis and high dose steroids. An intravenous urogram was performed using Urografin 58%, 2 ml/kg body weight. Tomography of the renal areas revealed smooth, enlarged kidneys with faint opacification of the central region of each kidney separated from an opacified outer rim by non-opacified cortex (Fig. 1). Further tomographic cuts revealed a faint pyelogram on the left side. Bilateral selective renal arteriography was performed and this demonstrated early capsular artery filling, poor opacification of the cortex and persistent filling of the segmental and lobar arteries (Fig. 2). The appearances were worse on

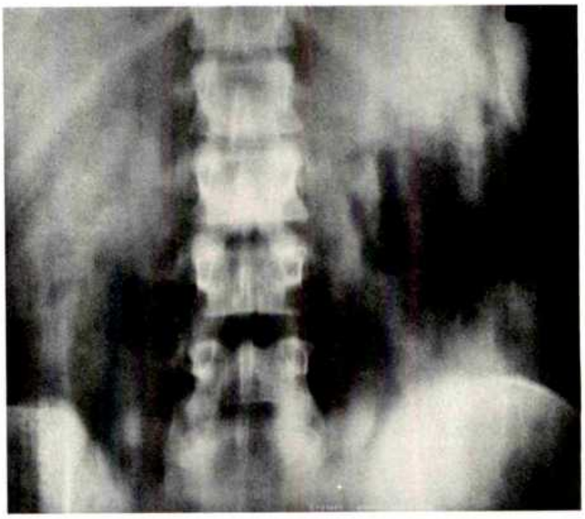


FIG. 1

Nephrotomogram. There is opacification of the margin of both kidneys and the central portions of the kidneys. A non-opacified zone of cortex is seen beneath the renal margin.

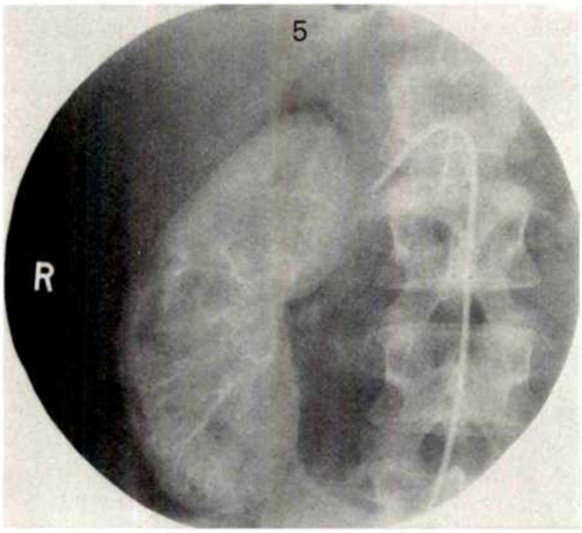


FIG. 2.

Selective renal arteriogram (late arterial phase). There is virtually no opacification of the cortex except for the outer rim. More centrally there is still persistent filling of the segmental and lobar arteries. Faint opacification of the renal vein is seen.

the right side. A diagnosis of renal cortical necrosis was made and the results of a renal biopsy were consistent with this diagnosis.

Further management was continued using haemodialysis via a leg shunt. She has since been followed up elsewhere and is maintained on home dialysis.

DISCUSSION

It has long been recognized that acute cortical necrosis may be patchy in nature and that a renal biopsy may therefore be inconclusive (Wells *et al.*, 1960). Several articles have pointed out the usefulness of performing selective renal angiography in patients with suspected acute cortical necrosis (Deutsch *et al.*, 1971; Kleinknecht *et al.*, 1973; Tuttle and Minielly, 1978). Typically the findings are: incomplete filling of the interlobular cortical arteries, marked filling of the capsular arteries and early venous filling. During the nephrographic phase the renal cortex is poorly opacified or shows a mottled appearance, the extent of cortical opacification being inversely proportional to the severity of the necrosis.

The reason postulated for this pattern of opacification is that an alternative blood supply exists for the subcapsular cortex, from capsular arteries which perforate the capsule and anastomose with the intrarenal vessels (Smith, 1963). These capsular vessels remain intact in acute cortical necrosis and some of the subcapsular cortex therefore remains viable. Similarly the juxtamedullary cortex and medulla remain viable since blood is shunted through the medulla which receives its blood supply from the modified glomerular vessels in the juxtamedullary region. This results in a pattern in arteriograms which is quite distinctive. There is opacification of the renal margin and of the medulla but absent or patchy opacification of most of the cortex.

It has generally been believed that intravenous urography in patients with cortical necrosis shows no contrast event, but Davidson (1977) suggested that with use of high dose nephrotomography renal opacification might be expected. Such opacification in three patients had already been reported in the French literature (Joffre *et al.*, 1976) and was similar in appearance to that seen during angiography, albeit to a diminished extent.

At least one other condition might be expected to give similar urographic appearances: acute incomplete obstruction to the renal artery due to an embolus. Selective functional cortical ischaemia in such a case has been reported (Siegelman and Goldman, 1968), arteriography showed opacification of the renal margin and of the medulla with absence of a cortical nephrogram. Apart from the presence of a filling defect in the renal artery due to the embolus the appearances were very similar to the arteriographic findings in acute cortical necrosis. It is therefore not unreasonable to assume that high dose nephrotomography might show appearances similar to those seen in our case and the cases reported by Joffre *et al.* (1976). It would however be extremely unusual for such a condition to affect both kidneys as is seen in acute cortical necrosis. Opacification of the renal margin has also been reported in a patient with renal infarction following repair of a large leaking aortic aneurysm (Frank *et al.*, 1974). Opacification of the renal margin was presumed to be the result of intact capsular perforating vessels, but apparently there was no medullary opacification and at postmortem examination there was total occlusion of both main renal arteries.

To what extent the opacification of the viable renal parenchyma in acute cortical necrosis is due to contrast in the proximal nephrons (filtered contrast) rather than a whole body opacification effect is debatable. The presence of a faint pyelogram on the left side in our case indicates continued glomerular filtration and the rather more patchy nature of the disease seen on the angiogram would tend to support this. In contrast the more severe and extensive necrosis on the right side together with absence of a pyelogram suggests that the whole body opacification effect rather than filtered contrast is responsible for the visualization of the renal parenchyma on this side. Whatever the cause of this opacification, this case demonstrates that with a high dose technique a nephrogram may be seen even in fairly severe acute cortical necrosis, and that the distinctive appearance of this nephrogram may aid in the earlier diagnosis of acute cortical necrosis.

ACKNOWLEDGMENTS

I would like to thank Professor T. Sherwood (Cambridge) and Dr. J. Goodwin (the London Hospital) for help and advice.

REFERENCES

DAVIDSON, A. J., 1977. *Radiologic Diagnosis of Renal Parenchymal Disease* (W. B. Saunders, Philadelphia), p. 149.

DEUTSCH, V., FRANKE, O., DRORY, Y., ELIAHOU, H. and BRAF, Z., 1971. Bilateral renal cortical necrosis with survival through the acute phase with a note on the value of selective nephroangiography. *American Journal of Medicine*, *50*, 828–834.

FRANK, P. H., NUTTALL, J., BRANDER, W. L. and PROSSER, D., 1974. The cortical rim sign of renal infarction. *British Journal of Radiology*, *47*, 875–878.

JOFFRE, F., DURAND, D., SABLAYROLLES, J. L., TEISSEIRE, R., PUTOIS, J. and SUC, J. M., 1976. Interêt de l'urographie intraveineuse au cours des nécroses corticales rénales. *Annals of Radiology*, *19*, 555–557.

KLEINKNECHT, D., GRÜNFELD, J., GOMEZ, P. C., MOREAU, J. and GARCIA-TORRES, R., 1973. Diagnostic procedures and long-term prognosis in bilateral renal cortical necrosis. *Kidney International*, *4*, 390–400.

1981, *British Journal of Radiology*, *54*, 526–528

SIEGELMAN, S. S. and GOLDMAN, A. G., 1968. The Trueta phenomenon: angiographic documentation in man. *Radiology*, *90*, 1084–1089.

SMITH, G. T., 1963. The renal vascular patterns in man. *Journal of Urology*, *89*, 275–288.

TUTTLE, R. J. and MINIELLY, J. A., 1978. The angiographic diagnosis of acute haemorrhagic renal cortical necrosis. *Radiology*, *126*, 637–638.

WELLS, J. D., MARGOLIN, G. and GALL, E. A., 1960. Renal cortical necrosis, clinical and pathological features in twenty one cases. *American Journal of Medicine*, *29*, 257–267.

Caroli's disease: its diagnosis with non-invasive methods

By Y. Imai, M.D., T. Watanabe, M.D., Y. Kondo, M.D. and F. Nakanishi, M.D.

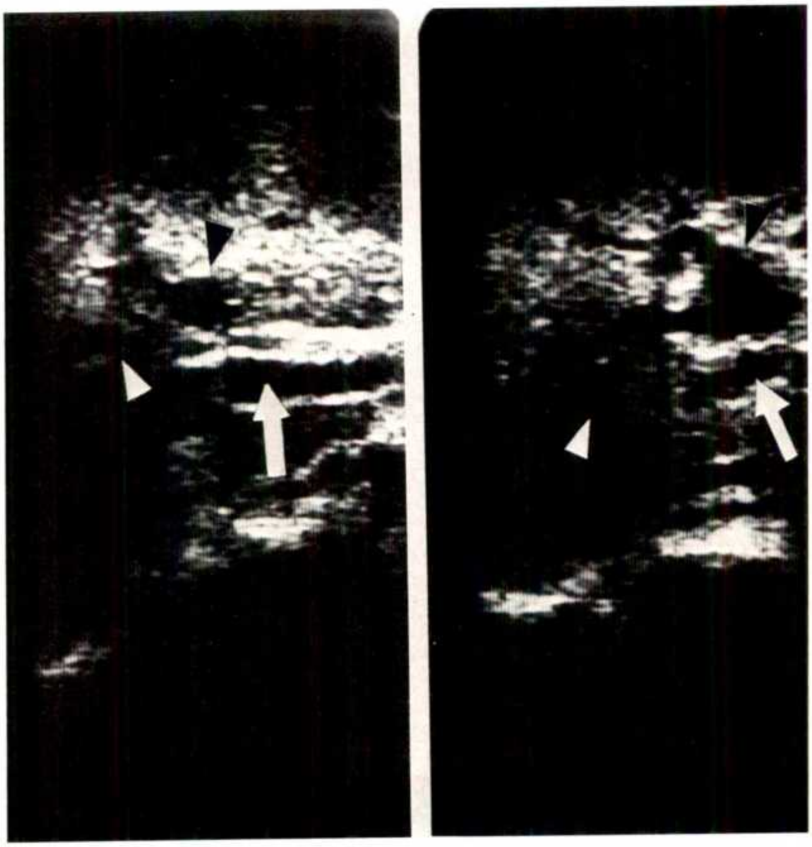
Department of Radiology, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano, Japan

(*Received July 1980*)

More than 50 cases of communicating cavernous ectasia of the bile duct have been reported. Diagnosis of this disease has been mainly by invasive methods such as percutaneous transhepatic or operative cholangiography. We were able to obtain a correct diagnosis pre-operatively using ultrasonography, ^{99}Tc^{m}-HIDA hepatobiliary scintigraphy and computed tomography. We wish to emphasize the usefulness of these non-invasive methods.

CASE REPORT

A 16-year-old girl was referred to the Shinshu University Hospital in September 1979 for low-grade fever, right hypochondralgia, anaemia and cyanosis with pain in the right toes. Systemic lupus erythematosus was diagnosed because of the presence of LE-cells and antinuclear antibodies. In



A FIG. 1. B

(A) Intercostal grey-scale ultrasonogram reveals two cystic sonolucent structures (indicated by arrowhead) anterior to the intrahepatic portal vein (indicated by arrow).

(B) Transverse scan reveals cystic structures more obviously.

November her serum alkaline phosphatase increased to 1500 mIU and her serum transaminases increased slightly (S–GOT 61 units, S–GPT 54 units).

An isotopic technetium-99m sulphur colloid scan revealed faint round defects extending over both lobes of the liver.

Intercostal and transverse grey-scale ultrasonograms were obtained with a Sonolayer SAC–12A digital scan converter using a 3.5 MHz transducer. Two cystic sonolucent structures were found anterior to the intrahepatic portal vein (Fig. 1). The gall bladder was found to be normal by another subcostal scan and no cystic lesions of the kidney were revealed.

A hepatobiliary scintigram with ^{99}Tc^{m}-HIDA 70 min after injection revealed retardation of excretion and two saccular dilatations of both intrahepatic bile ducts (Fig. 2). However, there was no dilatation of the common bile duct.

Computed tomography (CT) with EMI–5005 through the liver revealed two large saccular dilatations of the main intrahepatic bile duct which communicated with a small, round dilatation of the peripheral bile duct (Fig. 3). CT of the kidney after intravenous administration of contrast material revealed no cortical or medullary cysts.

These radionuclear, ultrasonographic and CT findings strongly suggested communicating cavernous ectasia of the biliary tract known as Caroli's disease.

Endoscopic retrograde cholangiopancreaticogram revealed saccular dilatation of the left main duct but failed to reveal the right one.

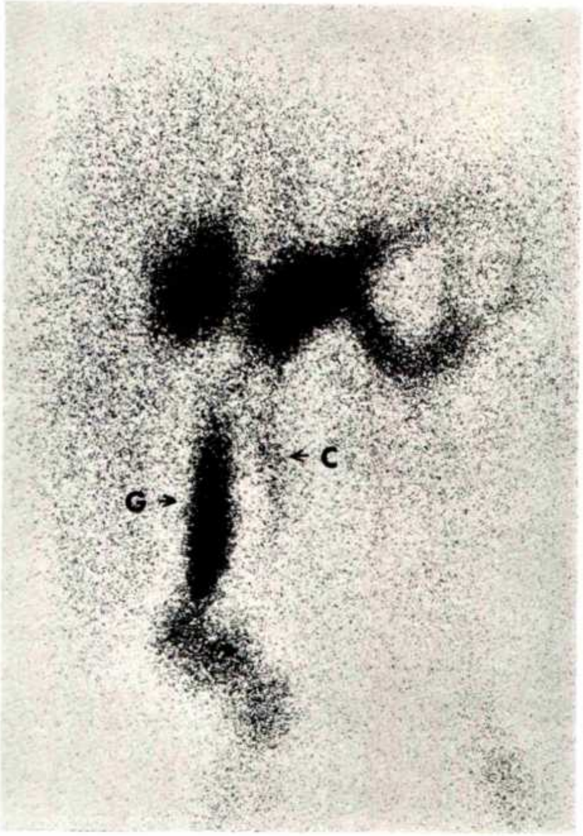


FIG. 2.

^{99}Tc^{m}-HIDA hepatobiliary scintigram 70 min after injection. Retardation of excretion and two saccular dilatations of the main intrahepatic bile ducts. "G" indicates gall bladder and "C" indicates common bile duct.

The patient was followed medically for two months, but she was readmitted in January 1980 because of increasing jaundice. Her total bilirubin was 12.4 mg/dl and her alkaline phosphatase was 5700 mIU. Laparotomy was done in February and the pre-operative diagnosis was confirmed. At this time numerous, small renal cortical cysts were observed bilaterally and many clumps of bile sludge were found in the

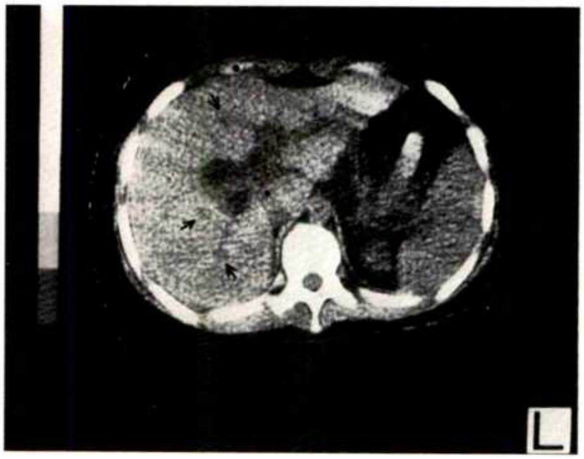


FIG. 3.

CT of the liver. Two large saccular dilations of the main intrahepatic bile ducts which communicate with dilatations of the peripheral bile ducts (indicated by arrows).

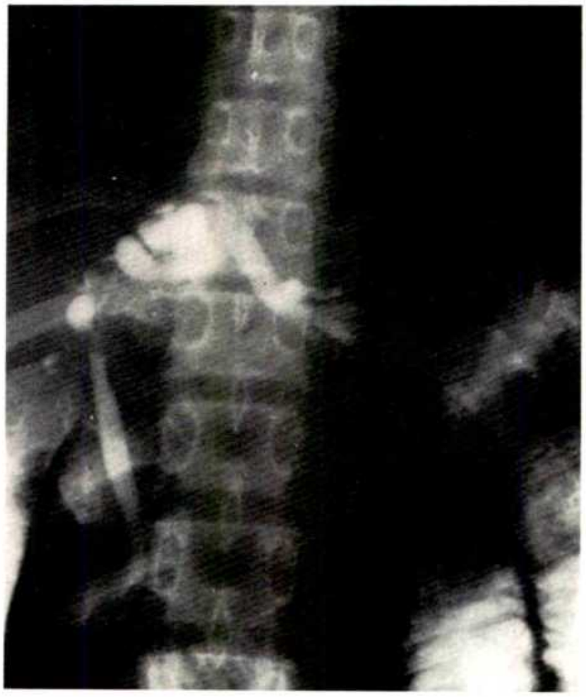


FIG. 4.

Endoscopic retrograde cholangiopancreaticogram reveals dilatation of the left main hepatic duct but fails to reveal the right one.

intrahepatic saccular cyst. These could not be diagnosed from the pre-operative examinations. A cholecystectomy and Roux-en-Y anastomosis between the wall of the saccular dilatation of the hepatic duct and jejunum and a liver biopsy were performed.

On the biopsy specimens of the resected cystic wall and choledochus, we could see submucosal fibrosis without inflammatory changes. The liver specimen showed interstitial fibrosis developing around the bile ducts in Glisson's capsule. Such fibrosis was different from that of chronic hepatitis and liver cirrhosis. Her bilirubin and alkaline phosphatase decreased subsequently after the operation.

DISCUSSION

More than 50 cases of communicating cavernous ectasia of bile ducts, known as Caroli's disease, have been reported since Caroli's first description (Caroli *et al.*, 1958). He classified this entity into two types: one was the pure form without hepatic cirrhosis or portal hypertension, the other was associated with congenital hepatic fibrosis (Caroli, 1968). The symptoms are cramp-like abdominal pain and fever due to stone formation and cholangitis, or gastrointestinal bleeding due to portal hypertension. According to Caroli (1973), jaundice does not occur, but a few cases with jaundice have been reported (Mall *et al.*, 1974; Bass *et al.*, 1977). The association with cystic renal lesions or medullary sponge kidneys is frequently reported (Reilly and Neuhauser, 1960; Kerr *et al.*, 1961; Rosewarne *et al.*, 1966; Foulk, 1970; Mujahed *et al.*, 1971; Mall *et al.*, 1974), and account for 60–80% of patients (Foulk, 1970). There is no report, to our knowledge, of associated systemic lupus erythematosus.

Pre-operative diagnosis of this disease has been difficult (Rosewarne *et al.*, 1966; Mujahed *et al.*, 1971; Bass *et al.*, 1977) and most diagnostic procedures have depended on invasive methods such as either percutaneous transhepatic cholangiography or operative cholangiography. The latter has been considered most useful (Watts *et al.*, 1974; Kaiser *et al.*, 1979). Concerning non-invasive methods, to our knowledge there have been two reports of ultrasonography (Bass *et al.*, 1977; Mittelstaedt *et al.*, 1980) and one of CT in the diagnosis of this disease (Kaiser *et al.*, 1979). Ultrasonography can demonstrate multiple large sonolucent cystic structures in the region of the porta hepatis. CT scan is able to demonstrate multiple-branching small low-density structures communicating with large round low-density areas, representing ectatic intrahepatic main bile ducts. Radionuclide liver scintigraphy is not generally useful except to reveal patchy uptake in the liver. ^{131}I rose bengal scintigraphy can reveal prolonged retention and slow drainage from the biliary ductal system (Mall *et al.*, 1974), but the precise location and extent of the disease cannot be detected satisfactorily. A hepatobiliary scintigram with ^{99}Tc^{m}-HIDA proved to be the most useful non-invasive method because it demonstrated the communication between the cystic dilatations of the intrahepatic bile ducts and common bile duct. Furthermore, it differentiated Caroli's disease from other liver cysts such as in polycystic disease and in congenital choledochal cyst associated with dilatation of the intrahepatic bile ducts.

We are convinced that the combination of ultrasonography, CT and ^{99}Tc^{m}-HIDA hepatobiliary scintigram is just as valuable, or more so, in the diagnosis of Caroli's disease than invasive methods such as percutaneous transhepatic cholangiography and/or operative cholangiography.

REFERENCES

BASS, E. M., FUNSTON, M. R. and SHAFF, M. I., 1977. Caroli's disease: an ultrasonic diagnosis. *British Journal of Radiology*, *50*, 366–369.

CAROLI, J., 1968. Disease of intrahepatic duct. *Israel Journal of Medical Science*, *4*, 21–25.

1973. Disease of intrahepatic biliary tree. *Clinics in Gastroenterology*, *2*, 147–161.

CAROLI, J., SPOUPAUT, R. and KOSSAKOWSKI, J., 1958. La dilatation polykistique congénitale des voies biliaires interhépatiques: essai de classification. *Semaine des hôpitaux de Paris*, *34*, 128–135.

FOULK, W. D., 1970. Congenital malformation of the intrahepatic biliary tree in the adult. *Gastroenterology*, *58*, 253–256.

KAISER, J. A., MALL, J. C., SALMON, B. J. and JACOB, J. P., 1979. Diagnosis of Caroli disease by computed tomography: report of two cases. *Radiology*, *132*, 661–664.

KERR, D. N. S., HARISSON, C. V. and SHERLOCK, S., 1961. Congenital hepatic fibrosis. *Quarterly Medicine*, *30*, 91.

MALL, J. C., GHAHREMANI, G. G. and BOYER, J. L., 1974. Caroli's disease associated with congenital hepatic fibrosis and renal tubular ectasia. *Gastroenterology*, *66*, 1029–1035.

MITTELSTAEDT, C. A., VOLBERG, F. M., FISCHER, G. J. and MCCARTNEY, W. H., 1980. Caroli's disease: sonographic findings. *American Journal of Roentgenology*, *134*, 585–587.

MUJAHED, Z., GLENN, F. and EVANS, J. A., 1971. Communicating cavernous ectasia of the intrahepatic ducts (Caroli's disease). *American Journal of Roentgenology*, *113*, 21–26.

REILLY, B. J. and NEUHAUSER, E. B. D., 1960. Renal tubular ectasia in cystic disease of the kidney and liver. *American Journal of Roentgenology*, *84*, 546–554.

ROSENWARNE, M. D., AKDAMER, K. and SPARKS, R. D., 1966. Congenital dilatation of the intrahepatic bile ducts. *American Journal of Medicine*, *40*, 188–194.

WATTS, D. R., LORENZO, G. A. and BEAL, J. M., 1974. Congenital dilatation of intrahepatic bile duct. *Archives of Surgery*, *108*, 592–597.

1981, *British Journal of Radiology*, 54, 529–530 JUNE 1981

Short communications

Potentiation of the radiation response of hypoxic mammalian cells by *cis*-dichlorobis(isopropylamine)trans-dihydroxy platinum IV (CHIP)

By M. Laverick, M.Sc., Ph.D. and A. H. W. Nias, D.M., F.R.C.R.

Richard Dimbleby Department of Cancer Research, St. Thomas's Hospital Medical School, London SE1

(*Received December 1980 and in revised form February 1981*)

Previous studies have shown that certain platinum coordination complexes can act as radiosensitizers *in vitro* and *in vivo*. *Cis*-dichlorodiamine-platinum II (*cis*-PDD), a potent antitumour agent now used in the clinic, acts as a radiosensitizer in both mammalian and bacterial systems (Richmond *et al.*, 1977; Douple and Richmond, 1978). Another platinum II complex, *cis*-dichlorobis (cyclopentylamine) platinum II (*cis*-PAD), potentiates damage due to X rays in well oxygenated Chinese hamster ovary (CHO) cells (Szumiel and Nias, 1976) and similar results were reported in a preliminary form for the platinum IV complex CHIP (Nias and Szumiel, 1977).

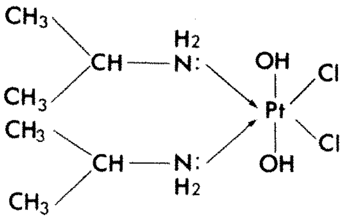
CHIP (see structure in Fig. 1) is one of eight platinum complexes selected from over 300 derivatives of *cis*-PDD as a possible second generation compound to follow *cis*-PDD into the clinic (Wilkinson *et al.*, 1978). CHIP is very soluble in aqueous solution and has a good therapeutic index (TI) of 12 as measured by Connors *et al.* (1971) (cf. *cis*-PDD with a TI of 8). This knowledge, together with the encouraging results of CHIP radiosensitization of well-oxygenated cells, has initiated the present investigation into the capabilities of CHIP as a hypoxic-cell sensitizer.

The experimental techniques have been described previously (Nias *et al.*, 1979). X rays of 212 kV were produced from a Maximar unit (HVL 1 mm Cu) and the dose rate was 1.85 Gy min^{-1}.

Figure 2 shows the results from a one hour pretreatment at 37°C of single C$_3$H mouse mammary tumour cells with 60 μg ml^{-1} (144μM) of CHIP, followed by irradiation under aerated or hypoxic conditions after different time intervals. Survival of colony-forming ability was assessed after seven days' incubation at 37°C.

The combined treatment data have been normalized with respect to the drug toxicity (60 μg ml^{-1} reduces survival to 50% of the control). Enhancement ratios (ER) were calculated from the ratio of the Do^3 values of the final slopes of the dose response curves for untreated and drug-treated cells, using data points with doses of 6 Gy and above (the final slopes were fitted by linear regression analysis). The OER for these cells was 2.7. The ER for cells treated with CHIP and then irradiated in air (□) is 1 (*i.e.* no potentiation at all). The ER for cells irradiated under hypoxia ia 2.1 at one hour after CHIP treatment (○), 1.14 with a five-hour interval (△), and 1.0 with an eight-hour interval (×) when the potentiating effect is lost.

CHIP appears to have a potentiating effect over the low and high dose range under hypoxic conditions but not in air. There is a decrease in the survival level in the "shoulder region", accompanied by a decrease in the final slope. At the one hour time-interval the survival over the low dose range is identical with that of cells irradiated under aerated conditions. This is of particular importance because the doses of radiation used in fractionated radiotherapy are similar to the lower end of the dose range used in these experiments (*e.g.* 2–4 Gy). If the potentiating effect was only observed over



Cis - dichloro-bis (isopropylamine) trans dihydroxy platinum (IV)

FIG. 1.

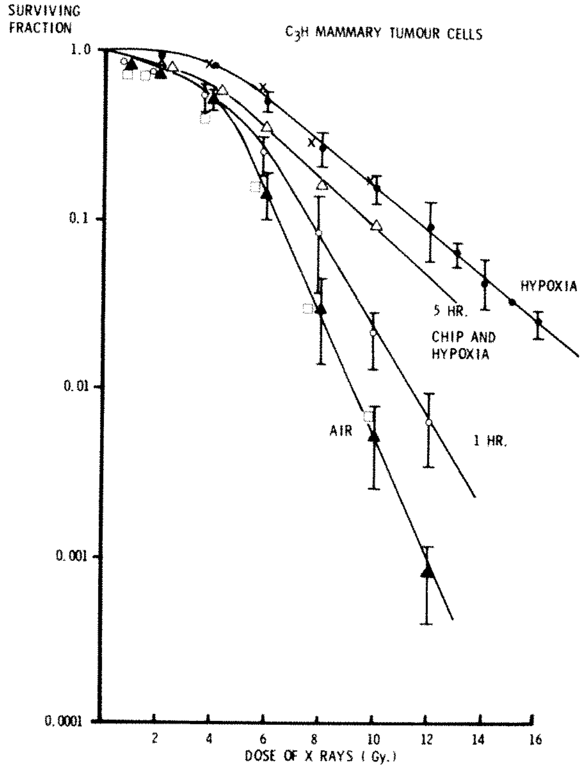


FIG. 2.

X-ray dose response curves for C$_3$H mouse mammary tumour cells X rays alone in air (▲, Do = 1.2 Gy, n = 18) and under hypoxia (●, Do = 3.3 Gy, n = 3.3). CHIP treatment one hour before X rays in air (□, Do = 1.2 Gy, n = 18). CHIP treatment before X rays under hypoxia; one hour interval (○, Do = 1.95 Gy, n = 3.9). Five hour interval (△, Do = 2.9 Gy, n = 2.8). Eight hour interval (×, Do = 3.3 Gy, n = 3.3). (Mean values from at least three experiments under each condition.)

1981, *British Journal of Radiology*, *54*, 530–532

the higher dose range (*i.e.* ≥6 Gy) there would be little or no clinical benefit.

Potentiating by CHIP is only observed after X irradiation under hypoxia. There will, therefore, be a greater possibility of achieving a higher therapeutic ratio using this type of combination therapy *in vivo*, where normal tissues are usually well oxygenated and the hypoxic regions are limited to the tumour mass.

The mechanism by which this enhancement of radiation damage is effected is not yet fully understood. The fact that under hypoxic conditions the "shoulder" region of the combined-modality dose–response curves is reduced suggests that either the accumulation or the repair of sublethal damage may be affected.

Pulse radiolysis of *cis*-PDD in aqueous solution by Richmond and Simic (1978) has shown that the platinum complex reacts rapidly with e^-aq., which under hypoxic conditions produces hydroxyl radicals and highly reactive platinum I intermediates, both of which can interact rapidly with important macromolecules such as DNA. This would have the effect of increasing the overall damage due to the platinum complex.

For the optimal operation of this mechanism the drug would have to be present during irradiation; in most sensitization studies where an ER has been reported a concurrent treatment of drug and irradiation has been employed (Alvarez *et al.*, 1978; Douple and Richmond, 1978; Stratford *et al.*, 1980). In one study the modifying effect was lost on removal of the drug from the bacterial suspension (Richmond *et al.*, 1977).

In the experiments reported here, when CHIP was given as a pretreatment to the cells followed by its removal from the culture medium, the maximum ER was found with a subsequent one hour delay before irradiation under hypoxic conditions. It would seem, therefore, that in this system cell/drug interaction plays an important part in the potentiation of damage by X rays, perhaps in affecting repair processes, and that the drug is not only acting as a target for the production of highly reactive intermediates as may be the case with other platinum II complexes.

Different time/dose regimes are now being investigated, including the concurrent treatment of cells with CHIP and X rays, in order to find the optimal condition necessary to produce the greatest potentiating effect.

ACKNOWLEDGMENTS

We would like to acknowledge the excellent technical assistance of Mr. A. Brock. This work was supported by a grant from the Cancer Research Campaign. CHIP was kindly supplied by Johnson Matthey & Co. Ltd.

REFERENCES

Alvarez, Ma V., Cobreros, G., Heras, A. and Lopez Zumel, Ma C., 1978. Studies on cis-dichlorodiammine platinum (II) as a radiosensitizer. *British Journal of Cancer*, *37*, *Supplement* III, 68–72.

Connors, T. A., Jones, M., Ross, W. C., Braddock, P. D., Khokhar, A. R. and Tobe, M. L., 1972. New platinum complexes with antitumour activity. *Chemico-biological Interactions*, *5*, 415–424.

Douple, E. B. and Richmond, R. C., 1978. Platinum complexes as radiosensitizers of hypoxic mammalian cells. *British Journal of Cancer*, *37*, *Supplement* III, 98–102.

Nias, A. H. W., Bocian, E. and Laverick, M., 1979. The mechanism of action of cis-dichloro-bis (isopropylamine) trans-dihydroxyplatinum IV (CHIP) on Chinese hamster and C$_3$H mouse tumour cells and its interaction with X-irradiation. *International Journal of Radiation Oncology Biology Physics*, *5*, 1341–1344.

Nias, A. H. W. and Szumiel, I. I., 1977. The effects of cis-dichlorobiscyclopentylamine platinum (II) PAD and cis-dichlorobisisopropylamine trans-dihydroxy platinum IV CHIP) and radiation on CHO cells. *Wadley Medical Bulletin*, *7*, 562–567.

Richmond, R. C. and Simic, M. G., 1978. Effect of radiation on cis-dichlorodiammine platinum (II) and DNA in aqueous solution. *British Journal of Cancer*, *37*, *Supplement* III, 20–23

Richmond, R. C., Zimbrick, J. D. and Hykes, D. L., 1977. Radiation induced DNA damage and lethality in *E. coli* as modified by the antitumour agent cis-dichlorodiammine platinum (II). *Radiation Research*, *71*, 447–460.

Stratford, I. J., Williamson, C. and Adams, G. E., 1980. Combination studies with misonidazole and a cis-platinum complex: cytotoxicity and radiosensitization *in vitro*. *British Journal of Cancer*, *41*, 517–522.

Szumiel, I. and Nias, A. H. W., 1976. The effect of combined treatment with a platinum complex and ionizing radiation on Chinese hamster ovary cells *in vitro*. *British Journal of Cancer*, *33*, 450–458.

Wilkinson, R., Cox, P. J., Jones, M. and Harrap, K. R., 1978. Selection of potential second generation platinum compounds. *Biochemie*, *60*, 851–857.

Induction of micronuclei by irradiation with neutrons produced from 600 MeV protons

By *I. Diehl-Marshall and M. Bianchi

CERN, Geneva, Switzerland

The induction of micronuclei is an easy, rapid and sensitive test that allows the evaluation of chromosome damage over a wide range of doses. For this reason it was chosen to determine the radiation damage caused by neutrons produced by 600 MeV protons. The neutrons had a wide energy spectrum, ranging from a few MeV up to 600 MeV. Because of this, a large variety of interactions can take place and a mixture of particles with high and low linear energy transfer (LET) is produced. The major part of the energy deposited at small depths comes from slow particles, while with increasing depth the contribution from high-energy particles increases rapidly.

We studied the radiation damage produced at the minimum achievable depth, where the contribution to the dose of slow secondary particles (high LET) is dominant. The damage was evaluated from the number of micronuclei produced.

Materials and Methods

The irradiations were made at a depth of 0.25 g/cm^2 in water, at a dose rate of about 20 cGy/h. Details of the beam parameters and dosimetry have been reported previously (Baarli *et al.*, 1977).

---

*Permanent address: Kernforschungszentrum Karlsruhe, Institut fur Kernphysik, 7500 Karlsruhe, Postfach 3640, Federal Republic of Germany.

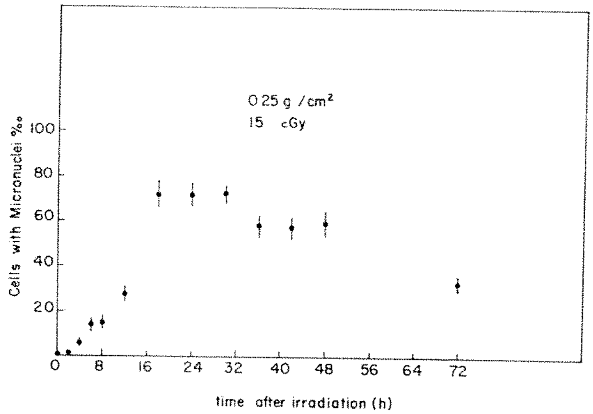


FIG. 1.

Number of cells with micronuclei at various time intervals after exposure to a dose of 15 cGy of neutrons.

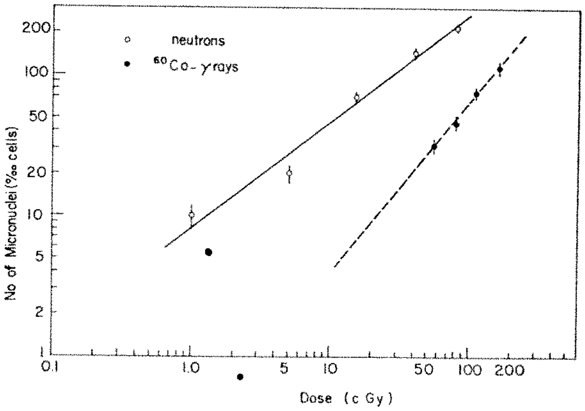


FIG. 2.

Average number of micronuclei between 24 and 48 hours after irradiation with a 600 MeV neutron beam and ^{60}Co γ rays.

Vicia faba bean roots were used for this experiment and selected for irradiation nine days after the dry seeds were put in water. Groups of beans were irradiated in aerated circulating water at 19°C with doses of 1, 5, 15, 41 and 82 cGy of neutrons. As a reference radiation ^{60}Co γ rays were used. Doses of 55, 80, 110 and 160 cGy were given at a dose rate of 150 cGy/h.

After irradiation the beans were transferred to growing tanks, where aerated tap water at 19°C was continuously added. Groups of three beans were fixed in alcohol–acetic acid solution: (3:1) at each of the various time intervals chosen. The last 1.5 mm of the root tip was stained using the Feulgen technique and permanent slides were made using the dry-ice method (Conger and Fairchild, 1963). In each of the three samples 1000 cells were analysed.

RESULTS AND DISCUSSION

The number of cells with micronuclei per 1000 cells at various times after irradiation is illustrated in Fig. 1 for a dose of 15 cGy of neutrons. The shape of this curve is quite representative of the trend observed for all other radiation doses given.

Micronuclei are formed from acentric fragments in the interphase following cellular division (Thoday, 1951; Gray and Scholes, 1951). If they are formed only after the first post-irradiation mitosis (M_1), their number should diminish immediately after the completion of the first cell cycle, owing to degeneration and dilution by undamaged cells. However, Fig. 1 shows a broad maximum between 24 and 48 hours after irradiation, suggesting that at least some micronuclei are also formed after the second post-irradiation mitosis (M_2). There are possibly two ways in which these "second wave" micronuclei are produced: (i) they could arise from fragments which were included in the daughter nuclei after the first mitosis (Scott and Evans, 1967) and (ii) if the DNA synthesis is involved in the processing of lesions leading to micronuclei (Griffiths and Carpenter, 1979), then cells which were in the G2 phase during irradiation could form micronuclei only after passing through M_2. As micronuclei can be produced in the second cell cycle after irradiation, the mean number of micronuclei observed during the period between 24 and 48 hours has been considered as a quantitative estimate of the radiation damage induced. The values obtained for irradiations with neutrons and ^{60}Co γ rays have been plotted versus dose in Fig. 2. The lines were obtained by a linear least-squares fit. A large variation of RBE with dose is evident from the figure. Extrapolation of the line for the γ-ray data gives RBE values varying from 3.5 at a dose of 82 cGy of neutrons, to 18 at 1 cGy, as indicated in Table I. The RBE values obtained from the extrapolation will underestimate the damage if there is a threshold dose for γ rays above 45 cGy.

TABLE I

RBE VALUES FOR THE NUMBER OF CELLS WITH MICRONUCLEI AND CELLS WITH MULTIPLE MICRONUCLEI

Neutron dose (cGy)	Cells with micronuclei	Cells with multiple micronuclei
1	18.0*	46.0
5	10.0*	18.0
15	6.7	9.3
41	4.5	5.4
82	3.5	3.7

*Extrapolated values.

Severe aberrations and cells with multiple chromosome damage have been found after irradiation with stopped negative pions (Gnanapurani *et al.*, 1972). This effect has been explained by the deposition of a large amount of energy in a cell or a group of cells by nuclear disintegration (star event). In the case of the high-energy neutrons used in the present experiment, a fraction of star events contribute to the absorbed dose as well. For this reason a separate analysis has been made of cells having more than one micronucleus. The results obtained are reported in Table I. The RBE values were 3.7 at a dose of 82 cGy of neutrons and 46 at 1 cGy.

The present results are in good agreement with evaluations made on opacification of the lenses of mice using the same neutron beam (Di Paola *et al.*, 1980). Variations of RBE between 5.8 at a dose of 41 cGy and 25.7 at 1 cGy were reported.

A correlation between the presence of micronuclei and the subsequent death of a cell has been found (Lea, 1962; Revell, personal communication, 1978). Therefore we tried to relate the number of cells containing micronuclei to the growth reduction in ten days. A complete loss of the proliferative capacity of the meristem ten days after irradiation is found when the total growth in ten days is reduced by

1981, *British Journal of Radiology*, *54*, 532–534

TABLE II

GROWTH ESTIMATE FROM INDUCTION OF MICRONUCLEI

Neutron dose (cGy)	Ten-day growth as % of control values from fitted line*	Expected growth from micronuclei (% of control)
1	99.0	97.5±0.2
5	95.0	94.9±0.7
15	85.6	82.2±1.5
41	65.9	65.0±2.0
82	42.9	49.4±3.1

*Taken from Bianchi and Diehl-Marshall (1981).

75%. This is reached with a dose of 130 cGy of neutrons (Bianchi and Diehl-Marshall, 1981). At this dose about 27% of the cells in the meristem contain micronuclei. An estimate of the expected percentage was made assuming a linear dependence on the percentage of cells containing micronuclei (X) of the form:

$$\text{Growth}=\left(100-\frac{75}{27}X\right).$$

This equation is valid for values of X between 0 and 27%. The computed results are found to be in good agreement with the experimental data, as shown in Table II.

The production of micronuclei has been shown to be a very suitable test for the evaluation of damage induced by radiation over a wide range of doses. This test can be used in radioprotection studies, where information on low-dose effects is scarce, and in radiotherapy to predict the number of cells that are going to be permanently damaged by a treatment.

ACKNOWLEDGMENTS

We would like to thank J. Baarli, C. Raffnsøe, D. Sotiriou, A. H. Sullivan and J. W. N. Tuyn for making the dosimetry measurements in the neutron beam. In addition we are indebted to A. H. Sullivan for evaluation of the doses and C. Raffnsøe for assistance during the γ-ray irradiations. We greatly appreciate the support of K. Panman, R. Paris and D. Williams in the biological preparations. Furthermore, we would like to thank the synchro-cyclotron group for providing the beam.

REFERENCES

BAARLI, J., BAKKE, O., SULLIVAN, A. H. and TUYN, J. W. N., 1977. Dosimetry studies in a 600 MeV neutron beam. *Proceedings of 3rd Symposium on Neutron Dosimetry in Biology and Medicine*, Munich, May 1977 (IAEA, Vienna), pp. 243–252.

BIANCHI, M. and DIEHL-MARSHALL, I., 1981. Effects of dose fractionation after irradiation with neutrons produced by 600 MeV protons. *British Journal of Radiology*, *54*, 532–534.

CONGER, A. D. and FAIRCHILD, L. M., 1963. A quick freeze method for making smear slides permanent. *Stain Technology*, *28*, 281–283.

DI PAOLA, M., COPPOLA, M., BAARLI, J., BIANCHI, M. and SULLIVAN, A. H., 1980. Biological responses to various neutron energies from 1 MeV to 600 MeV. 2. Lens opacification in mice. *Radiation Research*, *84*, 453–461.

GNANAPURANI, M., RAJU, M. R., RICHMAN, C. and WOLFF, S., 1972. Chromatid abberations induced by π mesons in *Vicia faba* root meristem cells. *International Journal of Radiation Biology*, *21*, 49–56.

GRAY, L. H. and SCHOLES, M. E., 1951. The effect of ionizing radiation on the broad bean root. *British Journal of Radiology*, *24*, 228–236.

GRIFFITHS, T. D. and CARPENTER, J. G., 1979. Premature chromosome condensation following X-irradiation of mammalian cells. Expression time and dose response. *Radiation Research*, *79*, 187–202.

LEA, D. E., 1962. *Action of radiations on living cells* (2nd edit.) (University Press, Cambridge).

SCOTT, D. and EVANS, H. J., 1967. X-ray induced chromosomal aberrations in *Vicia faba:* changes in response during the cell cycle. *Mutation Research*, *4*, 579–599.

THODAY, J. M., 1951. Effects of ionizing radiation on broad bean roots. Chromosome breakage and lethality of ionizing radiation by root meristems. *British Journal of Radiology*, *24*, 572–576.

Effects of dose fractionation after irradiation with neutrons produced by 600 MeV protons

By M. Bianchi and *I. Diehl-Marshall

CERN, Geneva, Switzerland

(*Received January 1980*)

Biological effects produced by neutrons of various energies up to 15 MeV have been extensively studied through their use in therapeutic applications (Barendsen, 1968; Hall *et al.*, 1973; Hornsey and Field, 1979). Possible further radiotherapeutic gains from neutrons of higher energies have been investigated recently (Harrison *et al.*, 1976; Hall and Durand, 1980).

Biological damage by neutrons with maximum energies of 400 and 600 MeV, produced by the CERN synchrocyclotron, have been investigated for several years. Unexpected effects were observed in the low-dose regions (Baarli *et al.*, 1976; Di Paola *et al.*, 1980; Diehl-Marshall and Bianchi, 1981).

These results have prompted more investigation to understand the mechanism of damage produced by neutrons at these energies. The study reported here is the first carried out on the effect of fractionation of neutron doses in the energy region of several hundred MeV.

MATERIAL AND METHODS

A neutron beam with a maximum energy of 600 MeV was used for the irradiations. Details of the beam characteristics and dosimetry have been reported previously (Baarli *et al.*, 1976; Baarli *et al.*, 1977). Irradiations were carried out at the minimum achievable depth in water (0.25 g/cm^2) and at

---

*Permanent address: Kernforschungszentrum Karlsruhe, Institut für Kernphysik, 7500 Karlsruhe, Postfach 3640, Federal Republic of Germany.

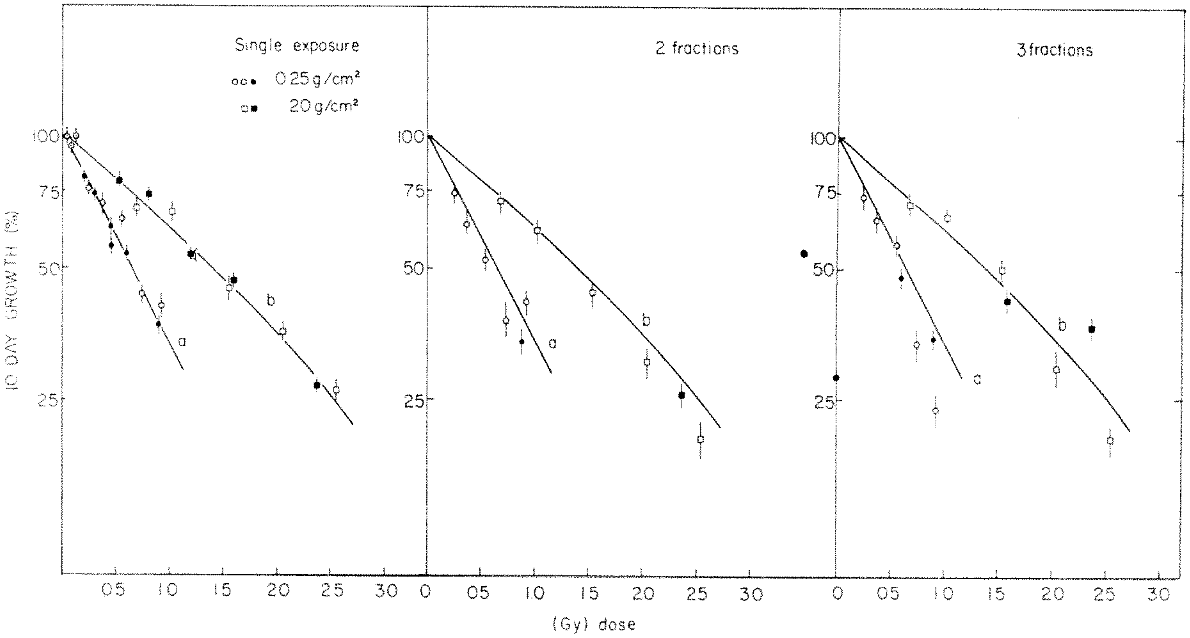


FIG. 1.

Percentage growth (with respect to the controls) after ten days following single and daily fractionated exposures to neutrons of maximum energy 600 MeV. The curves in the figures represent the best fit to the single-dose data. ○ and ●: 0.25 g/cm^2; □ and ■: 20 g/cm^2. Open and closed circles, open and closed squares indicate data from experiments done at different times.

a depth at which neutrons are in equilibrium with their secondaries (20 g/cm^2).

Vicia faba bean roots (variety Fillbasket) were irradiated. Nine days after the dry seeds had been put in water, roots of normal length and growth were selected for irradiation. Irradiations were carried out in aerated water at 19°C. After exposure, the beans were returned to the growing tanks, through which there was a continuous flow of aerated water. The length of the beans was measured daily for the subsequent ten days. Doses of 25 to 90 cGy were given at the minimal depth in water as single doses or divided into two or three equal daily fractions. The dose rate was about 20 cGy/h. Doses of 68 to 254 cGy were given to the roots at a depth of 20 g/cm^2. The dose rate was 56 cGy/h. Between 25 and 30 bean roots were irradiated per group.

RESULTS AND DISCUSSION

The results obtained from the growth during the ten days following the last irradiation are reported in Fig. 1 for the two irradiation positions. Experimental data from single- and fractionated-dose exposures have been fitted by the equation

$$G/G_0 = e^{-aD-bD^2} \quad . \quad . \quad . \quad (1)$$

where G_0 and G are the growth of unirradiated and irradiated roots respectively; a and b are constants; D is the dose of neutrons. A difference in the shapes of the curves for the two irradiation positions is observed. This can be ascribed to the qualitatively different composition of the beams. At the minimum depth, where the largest contribution to the dose is from short-range particles with high LET, the quadratic term of equation (1) become negligible.

The lines shown in Fig. 1 represent the best fit to single-dose exposures. From the curves fitted to single and fractionated exposures the dose ratio for various percentage growths was calculated. The values found for the minimum depths varied between 0.83 ± 0.11 and 0.9 ± 0.08 for two equal fractions given on successive days and between 0.8 ± 0.05 and 0.98 ± 0.12 for the three fractions spread over three days. This suggests that sensitization rather than recovery may have taken place.

At maximum build-up both the two-day and three-day fractionations gave about the same results as single-dose exposures. This indicates that a percentage of particles with high LET is sufficient to inhibit the recovery capacity of the cells.

So far no comparable data are available for γ rays at a similar dose rate. Data on recovery factors for a dose of 3 Gy given at 5 Gy/h indicated values of 1.28 and 1.61 for fractionation into two and three doses respectively. After 2.3 Gy the values were 1.57 and 1.44 (Bianchi *et al.*, 1980).

Irradiations made in the Bragg-peak region of a negative pion beam at a dose rate of about 5 Gy/h indicated that repair of the damage occurs if the two doses are given up to six hours apart. If the second dose was delayed by between 16 and 24 hours no recovery was visible. The damage was increased (recovery factor of 0.81) when the same dose was split into three equal doses given at one-day intervals (Bianchi *et al.*, 1980). The result is similar to the one reported in this paper.

Results obtained in a neon beam, with doses given at intervals of three hours using as assay intestinal crypts in mice (Goldstein and Phillips, 1979), and with 24 hour intervals using as assay the death rate of mice (LD 50/28) after irradiation of the oesophagus (Curtis, 1979), have also shown an enhanced effect by fractionation.

Differences between the experiments, and the scarcity of the data available, do not allow us to reach a conclusion on the origin of the sensitization effects observed. This subject needs further investigation because these results are relevant to the understanding of radiation effects.

ACKNOWLEDGMENTS

It is a pleasure for us to thank J. Baarli, leader of the Radiobiology Group at the time at which the experiments reported in both of these communications were carried out, for his support. We would like to thank J. Baarli, C. Raffnsøe, D. Sotiriou, A. H. Sullivan and J. W. N. Tuyn for making the dosimetry measurements in the neutron beam, A. H. Sullivan for the dose evaluations and M. Riedel for assistance given during the experiment. The skill and enthusiasm of R. Paris, K. Panman and D. Williams during the biological preparations and measurements is greatly appreciated. We are also indebted to the CERN SC Machine Group.

REFERENCES

BAARLI, J., BIANCHI, M. SULLIVAN, A. H. and DI PAOLA, M., 1976. Biological effects of hadrons at very low doses. *Proceedings of the International Symposium on Biological and Environmental Effects of Low-Level Radiation*, Chicago, 1975 (IAEA, Vienna), Vol. 1, pp. 195–204.

BAARLI, J., BAKKE, O., SULLIVAN, A. H. and TUYN, J. W. N., 1977. Dosimetry studies in a 600 MeV neutron beam. *Proceedings of the 3rd Symposium on Neutron Dosimetry in Biology and Medicine*, Munich, 1977 (IAEA, Vienna), pp. 243–252.

BARENDSEN, G. W., 1968. Responses of cultured cells, tumours and normal tissues to radiations of different linear energy transfer. *Current Topics in Radiation Research*, *4*, 293–356.

BIANCHI, M., DIEHL, I., BAARLI, J. and SULLIVAN, A. H., 1980. Dose fractionation effects with negative pions. *British Journal of Radiology*, *53*, 509–510.

CURTIS, S. B., 1979. Biological properties of heavy ions. *Proceedings of the Sixth International Congress of Radiation Research*, Tokyo, 1979 (eds. M. Terashima and Y. Yamaguchi), pp. 780–797.

DIEHL-MARSHALL, I. and BIANCHI, M., 1981. Induction of micronuclei by irradiation with neutrons produced from 600 MeV protons. *British Journal of Radiology*, *54*, 530–532.

DI PAOLA, M., COPPOLA, M., BAARLI, J., BIANCHI, M. and SULLIVAN, A. H., 1980. Biological responses to various neutron energies from 1 MeV to 600 MeV. 2. Lens opacification in mice. *Radiation Research*, *84*, 453–461.

GOLDSTEIN, L. S. and PHILLIPS, T. L., 1979. Recovery of the reproductive integrity by jejunal crypt cells following fractionated irradiation with accelerated heavy ions or pions. *Abstracts of the Sixth International Congress of Radiation Research*, Tokyo, 1979, p. 159.

HALL, E. J., ROSSI, H. H. and KELLERER, A. M., 1973. Radiobiological studies with monoenergetic neutrons. *Radiation Research*, *54*, 431—443.

HALL, E. J. and DURAND, R. E., 1980. Oxygen enhancement ratio for high-energy neutrons. *British Journal of Radiology*, *53*, 166.

HARRISON, C. H., KUBICZEK, E. B. and ROBINSON, J. E., 1976. OER reduction with high-energy neutrons. *British Journal of Radiology*, *49*, 733.

HORNSEY, S. and FIELD, S. B., 1979. Biological properties of neutrons relevant to neutron therapy. *Proceedings of the Sixth International Congress of Radiation Research*, Tokyo, 1979 (eds. M. Terashima and Y. Yamaguchi), pp. 762–770.

Long-term observation of mouse foot reaction after hyperthermia: hyperthermia may or may not be carcinogenic?

By M. Urano, M.D., Ph.D.

Department of Radiation Medicine, Massachusetts General Hospital, Harvard Medical School,
Boston, Ma, 02114, USA

(Received June 1980 and in revised form January 1981)

A renewed interest in hyperthermia as a potential method of cancer therapy has stimulated biological studies on the thermal effect. We have studied the response of animal tumours and normal tissues to elevated temperature. In a series of experiments, animals which had received hyperthermia to their feet were observed until their spontaneous death in order to investigate possible hyperthermic late effects including carcinogenesis.

The animals were C3Hf/Sed mice derived from our defined flora colony. They were kept in our animal facility where the defined flora conditions were maintained. The tumour was a 4th generation isotransplant of a methylcholanthrene-induced fibrosarcoma (FSa-I) which was moderately immunogenic (Suit *et al.*, 1976). Tumours were treated at an average diameter of 6 mm. Hyperthermia was given by immersing the feet in a water bath where 43.5 ± 0.1 °C was maintained by a Haake Model E-52 constant temperature circulator (West Germany). Each mouse was held in an individual holder without anaesthesia. The right foot was kept in position by taping the hind leg to a flat holder arm which was wider than the animal's leg. This procedure did not cause occlusion of the blood vessels. A total of 113 mice were used. Among them, 58 received single treatment to their normal feet and 55 received treatment to tumour-bearing feet. Animals which developed recurrences (12 mice) or metastases (two mice) were excluded from this study. Therefore, a total of 99 mice were observed until death. These animals, including tumour bearing and non-tumour bearing animals, received hyperthermia alone (46 mice) or hyperthermia following systemic administration of 350 μg *C. parvum* (53 mice). Treatment time at elevated temperature varied from 30 to 210 minutes.

After treatment the reaction in the foot of non-tumour bearing animals was numerically scored every day for the first four weeks, once a week for the next three months, and once every other week thereafter. The scoring system and the dose-response relationship have been described elsewhere (Urano *et al.*, 1978). Tumour-bearing animals were observed for possible tumour recurrence and the foot reaction was recorded as well. The total observation period was approximately 950 days.

Some typical courses of development of the foot reaction are presented in Fig. 1. All the reactions developed very rapidly within the first 30 days and the reversible skin reaction (score $\leqslant 3.5$) gradually subsided thereafter. The recovery of the foot reaction appeared to be incomplete for a reaction > 2.0. The only recognizable late finding was telangiectasia which developed exclusively on the amputated (*i.e.*, $\geqslant 5.0$) margin of the foot 11–12 months after hyperthermia. There were 47 mice which showed severe moist desquamation with some degree of necrosis (score $\geqslant 4.0$) and another 17 mice developed a reaction ranging from severe oedema with complete epilation to moist desquamation on an entire foot (Table I). However, none of the animals

---

This work was supported by Grant CA26350 from the National Cancer Institute, Department of Health, Education and Welfare.

TABLE I

THE DISTRIBUTION OF ANIMALS DEVELOPING VARIOUS PEAK FOOT REACTIONS AFTER LOCAL HYPERTHERMIA TO THE FOOT

Score of peak foot reaction	Signs	Number of animals		Total
		Heat alone	*C. parvum* + heat	
< 2.0	< complete epilation	12 (5)*	23 (19)	35 (24)
2.0–3.5	< total moist desquamation	10 (3)	7 (3)	17 (6)
4.0–4.5	loss of toe(s)	15 (8)	6 (1)	21 (9)
> 4.5	> partial loss of foot	9 (2)	17	26 (2)
Total		46 (18)	53 (23)	99 (41)

*Numbers in parentheses indicate number of animals treated with foot tumours without recurrence.

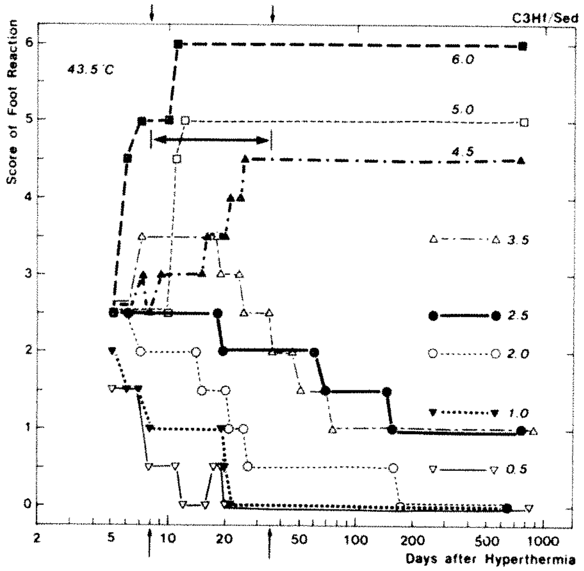


FIG. 1.

Scores of foot reaction in eight mice as a function of time after hyperthermia. Early reactions were scored between day eight and 35 as indicated by arrows. Each curve represents the foot reaction in a single animal which developed a typical "peak foot reaction score". Numbers indicate the peak foot reactions.

TABLE II

CAUSE OF DEATH*

Cause of death	Number of animals		Total
	Heat alone	*C. parvum* + heat	
Spontaneous tumours†	14	20	34 (34.3%)
Ovarian cysts or tumours	5	7	12 (12.1%)
Liver diseases	7	7	14 (14.1%)
Others	20	19	39 (39.4%)
Total	46	53	99

*Animals which developed recurrences or metastases are not included in this study.

†Including mammary carcinoma. No tumour developed in treated or untreated feet.

developed a new tumour in the treated area. Also no tumour was observed in animals with scores ranging from no reaction (score 0) to partial epilation or oedema (score ⩽ 1.5). The tumours were controlled with a resultant scar formation from which no secondary neoplasms arose.

The cause of death included spontaneous malignant tumours (34%), ovarian cysts (12%), liver diseases (14%), and others (other diseases and unidentified) (Table II). No tumours developed in untreated feet. Median survival times after hyperthermia alone and combined treatments were 760 (712–811) and 752 (699–808) days respectively. No difference was observed in the cause of death or median survival time between animals treated with heat alone and those treated with *C. parvum* and heat.

One of the serious problems associated with cancer treatment is the development of late damage including secondary neoplasms. Radiation is a well-known carcinogen and the development of leukaemia is not infrequent after systemic chemotherapy. Although no studies on radiation-induced tumours on the mouse foot have been reported to our knowledge, we observed a high incidence of malignant neoplasms secondary to radiotherapy of transplanted leg tumours in C3Hf mice (Urano *et al.*, 1979). These neoplasms developed only in irradiated legs, *i.e.*, between ankle and the proximal portion of the thigh. Similar results were also reported by Suit *et al.* (1977). In these reports, no spontaneous tumours were observed in untreated legs or feet. In contrast, the present experiment suggests insignificant carcinogenic effects of hyperthermia. The present result is supported by two separate *in vitro* experiments which demonstrated no possible transformation in heated mammalian cells (Clark, personal communication; Harisiadis *et al.*, 1980). A wide range of treatment times which induced a variety of foot reactions was examined in the present study (Table I). The damage induced by mild hyperthermia might be repairable while those induced by severe treatment might involve extensive cell killing. Notably, no type of foot reaction was associated with secondary neoplasms.

The so-called scar cancer or Marjolin's ulcer which develops in a burn scar is occasionally reported in the literature. In a review article the incidence of scar cancer of the skin is estimated to be between 0.1 and 2.59% among patients with carcinoma of the skin (Coburn, 1976). Although a precise figure is not available for the incidence of scar cancers because of lack of significant statistical data, these clinical observations obviously contradict experimental evidence and suggest a possible carcinogenic effect of hyperthermia. It is notable, however, that some early experimental studies support the two-stage theory of carcinogenesis, the burn being the initiating agent and the subsequent treatment the promoting factor (Coburn, 1976). Thus, the application of a chemical or physical carcinogen to the burned tissue could promote the development of malignant neoplasms (Castillo and Goldsmith, 1968; Saffiotti and Shubik, 1956; Simpson, 1947). It is unknown if the tissue damage following hyperthermia (moderate temperature) and that caused by an experimental burn (high temperature) are comparable, but these early experiments apparently suggest that hyperthermia, if followed by other treatment modalities which have carcinogenic potential such as radiation or chemotherapy, could induce secondary neoplasms, although the hyperthermia alone appears to be an extremely weak carcinogen. Studies on this subject should be undertaken.

REFERENCES

CASTILLO, J. and GOLDSMITH, H. S., 1968. Burn scar carcinoma. *CA: A Cancer Journal for Clinicians*, *18*, 140–142.

COBURN, R. J., 1976. Malignant ulcers following trauma. In *Cancer of the Skin: Biology, Diagnosis, Management*. Ed. R. Andrad, S. L. Mumport, G. L. Popkin and T. D. Rees (W. B. Saunders, Philadelphia), ch. 41, pp. 939–949.

HARISIADIS, L., MILLER, R. C., HARISIADIS, S. and HALL, E. J., 1980. Oncogenic transformation and hyperthermia. *British Journal of Radiology*, *53*, 479–482.

SAFFIOTTI, U. and SHUBIK, P., 1956. The role of burning in carcinogenesis. *British Journal of Cancer*, *10*, 54–56.

SIMPSON, W. L., 1947. An experimental study of single trauma malignancy. *Cancer Research*, *7*, 726.

SUIT, H. D., SEDLACEK, R., WAGNER, M., ORSI, L., SILOBRCIC, V. and ROTHMAN, K. J., 1976. Effect of *Corynebacterium parvum* on the response to irradiation of a C3H fibrosarcoma. *Cancer Research*, *36*, 1305–1314.

SUIT, H. D., HOWES, A. E. and HUNTER, N., 1977. Dependence of response of a C3H mammary carcinoma to fractionated irradiation on fractionation number and intertreatment interval. *Radiation Research*, *72*, 440–454.

URANO, M., OVERGAARD, M., SUIT, H., DUNN, P. and SEDLACEK, R., 1978. Enhancement by *Corynebacterium parvum* of the normal and tumor tissue reponse to hyperthermia. *Cancer Research*, *38*, 862–864.

URANO, M., KOIKE, S. and OHARA, K., 1979. Secondary malignant neoplasms following radiotherapy of a mouse mammary carcinoma. *Cancer*, *43*, 151–156.

Book review

Biology of Ovarian Neoplasia. (A Series of Workshops on the Biology of Human Cancer Report No. 11). Ed. by E. D. Murphy and N. G. Beamer, pp. 132, 1980 (UICC, Geneva) Sw. fr. 16.00.
ISBN 92-9018-050-1

This is one of a series of reports published by the Union Internationale Contre Le Cancer and details the papers and discussions of a workshop on ovarian cancer held in Geneva in 1979. It gives an up-to-date report on the present understanding of the causes, pathogenesis and pathophysiology of the main types of human ovarian cancer. Particular emphasis is given to the evaluation of basic animal models.

This book is of interest not only to scientists but also to clinicians treating ovarian cancer. In particular the chapter by H. Fox, "Human ovarian tumours: classification, histogenesis, pathogenesis, and criteria for experimental models", and the chapter by N. S. Weiss, 'Epidemiology of ovarian cancer', should reach a far wider audience.

The problems relating to animal models for tumours of the ovary are well reviewed and a good model for studying ovarian teratomas in mice is reported by L. C. Stevens. Animal models are helpful in the study of sex cord stromal tumours, but at the present time we are a very long way from having ideal animal models for studying the all too common epithelial tumours of the ovary.

The hypothesis that gonadotrophins are significant factors in ovarian tumorgenesis is emphasized in several of the papers and E. D. Murphy makes the interesting suggestion that their measurements might lead to recognizing women at risk. Several other tumour markers, including CEA and AFP, while not suitable for screening to improve earlier diagnosis, may be useful in the management of cancer patients, but the need for better markers to be isolated is essential for improved monitoring of patients with ovarian cancer. Sensitivity testing of ovarian tumours for the assessment of cytoxic drugs in an individual patient *in vitro* is detailed, but again many problems need to be solved before this can become a routine procedure.

The book ends with a short chapter on suggested goals for further research. It is obvious that very much more fundamental research is required in all aspects of the biology of ovarian neoplasia. The enormous amount of work that is still required to be done in this field will take many years. These basic biological data are essential if clinical work in the future is to improve the prognosis of patients with ovarian carcinoma.

HANNAH LAMBERT.

1981, *British Journal of Radiology*, *54*, 537–538

JUNE 1981

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Excretion of metrizamide in milk

THE EDITOR—SIR,

Metrizamide (2-{[3-(acetylamino)-5-(acetylmethylamino)-2,4,6-triiodobenzoyl]amino}-2-deoxy-*D*-glucose) is a water-soluble non-ionic, radiographic contrast medium used mainly in myelography. After intrathecal or subarachnoid administration, the drug is absorbed into the blood (Golman, 1975) and is excreted unchanged in the urine with 55–96% of the dose being recovered in 24 h (Hindmarsh, 1973; Golman, 1975). The drug is not recommended for use in nursing mothers since neither its excretion in milk nor its effects in the new-born have been investigated.

We have studied the pharmacokinetics of metrizamide in a 38-year-old woman (71.5 kg) with signs of root compression in the lower cervical segments. A cervical myelogram was performed in which 5.06 g metrizamide were injected into the subarachnoid space. Serial blood samples, all urine excreted and all milk expressed were collected at intervals for a period of 48 h and metrizamide concentration was measured by high-performance liquid chromatography (HPLC). Briefly, blood, serum or milk (0.2–0.5 ml) and urine (0.1 ml of a 1:10 dilution in water) were mixed with acetonitrite (1:5 or 1:10) containing phenobarbitone (6 μg) as internal standard. After centrifugation, 0.5–4 ml of the supernatant were evaporated to dryness, redissolved in 100 μl of the HPLC mobile phase and 10–20 μl aliquots injected onto the column. The HPLC conditions were as follows: C_{18} μ-Bondapak column (4 mm i.d. × 30 cm, Waters Associates, Aust.) a mobile phase of 9.5% methanol in 0.07 M phosphate buffer (pH 8) pumped at 2 ml/min and detection of eluted drug peaks at 254 nm. Under these conditions, metrizamide and phenobarbitone chromatograph with retention times of about 7 and 12 min respectively. Metrizamide concentration in plasma was 12 μg/ml 1 h after dosing, a peak concentration of 32.9 μg/ml was measured at 6 h and levels then slowly decreased to 2.7 μg/ml at 48 h (Fig. 1). Blood concentrations were considerably lower at all times (mean red cell/plasma ratio = 0.16) indicating that the drug does not readily penetrate the red cell membrane (Fig. 1). When fitted to a one-compartment open model with first-order absorption, the plasma data were well described by an absorption rate constant of 0.2 h^{-1} (absorption half-time = 3.5 h), a volume of distribution of 91 l and an elimination rate constant of 0.07 h^{-1} (half-life = 10.1 h). The elimination half-life is similar to previously reported values (Golman, 1975; Kullberg *et al.*, 1979). Cumulative urinary excretion of metrizamide was low in the first 12 h after dosing when urine flow was also low (8–38 ml/h). These small urine volumes may be partly attributed to nausea and vomiting which the patient experienced in the first few hours after dosage but could also be due to urinary retention which has previously been reported for metrizamide (Skalpe, 1977). However by 24 h urine flow had increased to 102 ml/h and by 44.3 h some 68% of the dose had been recovered in the urine (Fig. 2). Cumulative excretion in milk increased linearly with time (Fig. 2) but was extremely small

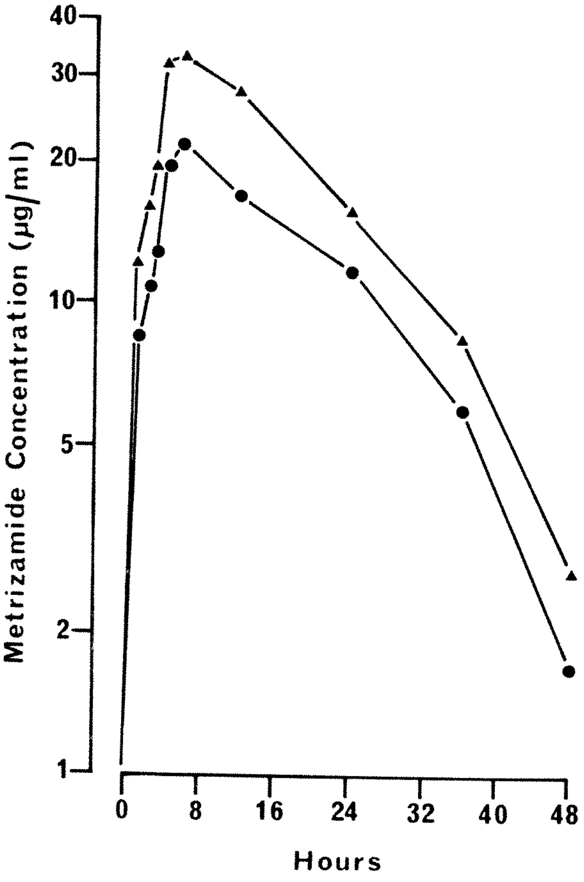


FIG. 1.

Metrizamide concentration in blood (●—●) and plasma (▲—▲).

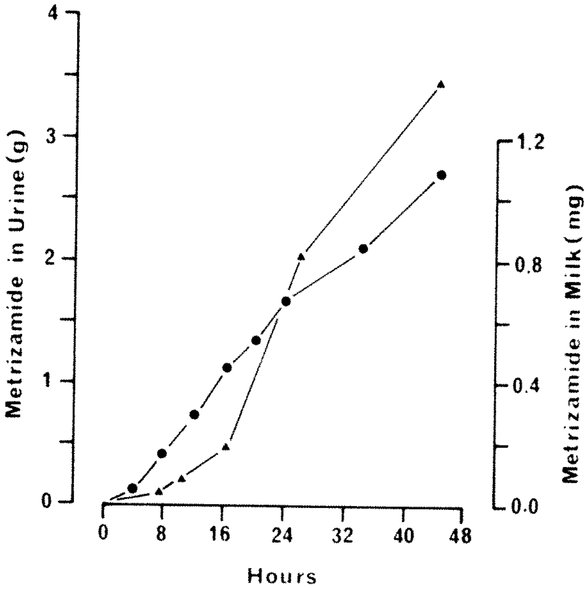


FIG. 2.

Cumulative excretion of metrizamide in urine (▲—▲) and milk (●—●)

1981, *British Journal of Radiology*, *54*, 538–539

with only 1.1 mg or 0.02% of the dose being recovered in 44.3 h. This is in agreement with the known mechanisms for drug excretion in milk (Vorherr, 1974) which predict a low rate of excretion for metrizamide since it is non-ionized, extremely water soluble and has a high molecular weight (789). The concentration of metrizamide in milk was significantly correlated to that in blood ($r = 0.74$, $P < 0.05$) indicating that blood concentration is an important factor in determining its extent of excretion in milk.

We suggest that the very small amount of metrizamide excreted in milk is of itself unlikely to be a hazard to the breast-fed infant unless the infant is hypersensitive to the drug.

Yours, etc.,
K. F. Ilett,
L. P. Hackett,
J. W. Paterson.

Combined Unit in Clinical Pharmacology and Toxicology,
Queen Elizabeth II Medical Centre,
Shenton Park, 6008, Western Australia.

C. C. McCormick.

St. John of God Hospital,
Subiaco 6009, Western Australia.

(*Received February 1981*)

REFERENCES

Golman, K., 1975. Absorption of metrizamide from cerebral spinal fluid to blood: pharmacokinetics in humans. *Journal of Pharmaceutical Sciences*, *64*, 405–407.

Hindmarsh, T., 1973. Elimination of water-soluble contrast media from the subarachnoid space. *Acta Radiologica*, Supplement *346*, 45–50.

Kullberg, M. P., Biddlecome, C. E., Ross, R. W. and Edelson, J., 1979. High-performance liquid chromatographic determination of metrizamide in plasma. *Journal of Chromatography*, *168*, 533–537.

Skalpe, I. O., 1977. Adverse effects of water soluble contrast media in myelography, cisternography and ventriculography. A review with special reference to metrizamide. *Acta Radiologica*, Supplement *355*, 359–370.

Vorherr, H., 1974. Drug excretion in breast milk. *Postgraduate Medicine*, *56*, 97–104.

Strategic marking in MCQ papers

The Editor—Sir,

The usual advice given to candidates attempting MCQ examination papers is to tick those answers which they are certain or fairly certain are correct and leave blank the ones they are unsure about. An alternative strategy, the details of which are set out below, is to ensure that every question is answered whether the candidate knows the answer or not. Users of the first type of strategy are referred to below as "chickens" and users of the second type of strategy as "gamblers". It is clearly in the interests of a "fair" examination that all candidates should use the same marking strategy when answering the questions, so it is not surprising that teachers tend to encourage the "chicken" approach rather than the "gambler" approach since the latter may introduce spurious changes in examination results. Some candidates may enter this contest so supremely confident of their ability to score a high proportion of "certain correct" answers that they can afford to guarantee themselves as a zero score on the remaining questions. However, I would expect most candidates to be anxious to take advantage of any legal answer-marking strategy which improves their overall score. The aim of the "gambler's" strategy is to improve his or her overall score by a few per cent which in the case of a border-line candidate may be enough to take him clear of the pass mark.

The "gambler's" strategy detailed below is designed for the F.R.C.R. multiple-choice examinations. Under existing regulations the following information is given to each candidate:

(a) There are 60 questions, each of five parts.
(b) Each part has a correct answer, either "yes" or "no".
(c) In each group of five parts there is at least one correct "yes" answer and at least one correct "no" answer.
(d) For each part-answer marked correctly the candidate will be awarded one mark; for each answer marked incorrectly the candidate will be awarded minus one mark; failure to mark either "yes" or "no" will result in zero marks being awarded for that answer.

Both "chickens" and "gamblers" will first tick off the "yes" and "no" answers which they are sure are correct. They will then review the remaining blank spaces on the answer sheet. It will be immediately obvious that if four "yes" or four "no" answers have been already ticked in a single question then the remaining answer must be "no" or "yes" respectively since the candidates are told that there are no five/zero or zero/five splits between yes/no answers in any one question. "Chickens" will stop at this point and rest on their laurels secure in the knowledge that they have not risked scoring minus points by wrong guesses. For "gamblers" however this is where the story really starts. The aim of the "gambler" strategy is to fill in all the vacant spaces remaining on the answer sheet in such a way that more than half of the guesses will be correct. This is actually easier than it first appears. The strategy is based upon three points, the first of which depends upon the overall frequency of "yes" and "no" correct answers. In order to avoid spurious gains by candidates systematically over-marking "yes" answers ("optimism") or "no" answers ("pessimism") it is desirable to have approximately equal numbers of "yes" and "no" answers in the paper as a whole. The candidate can then use this expectation to indicate the likely probability of his answers being "yes" or "no". For example, say the candidate has answered correctly 150 of 300 possible question parts. He then counts the number of "yes" and the number of "no" answers he has made. If he finds that he has marked 100 answers "yes" and 50 answers "no", he may then assume that of the 150 answers remaining to be marked, 100 should be "no" and 50 "yes", *i.e.* any individual blank space remaining is twice as likely to have a correct "no" answer as a correct "yes". If the candidate were then to mark all his blank spaces with the answer "no" he would expect to score about 100 plus marks and 50 minus marks, thus improving his score by about 17% over that which he would have had if he had followed the "chicken" strategy of leaving unknown answers blank.

The second part of the strategy is based on the distribution of yes/no answers within each group of five question parts. We are told that there are no five/zero splits in any question and therefore the only possible splits are four/one or three/two. If equal numbers of correct "yes" and "no" answers are distributed randomly amongst the 300 question parts the number of three/two splits will be approximately twice as great as the number of four/one splits *i.e.* out of 60 questions there should be approximately 40 three/two splits and approximately 20 four/one splits. This knowledge may help the candidate to fill in a number of his blank spaces; for instance if there are a few questions in which he has filled four out of the five answer parts with three "yeses" and one "no", it is twice as likely that the remaining answer will be "no" (giving a three/two split) as "yes" (giving a four/one split). The third point in the strategy arises from the empiric observation that the distribution of yes and no answers across the five answer columns "a" to "e" may be skewed. This could be accounted for by the tendency when creating multiple choice questions first to write in correct alternatives and then to make up the number of question parts to the required five by subsequently adding incorrect alternatives. The examiners could counter this by randomizing the order in which each group of five question parts was printed; it is however worth checking whether or not this has been done by adding up the numbers of certain-correct "yes" and "no" answers in each of the columns "a" to "e". It was found on one occasion, for example, that two-thirds of the correct answers in columns "a" and "b" were "yes" and two-thirds of the correct answers in column "d" and "e" were "no", with an equal split of "yes" and "no" answers in column "c". Any such inequality of distribution between the five columns provides the candidate with a third factor in his attempt to correctly guess more than half of the unanswered questions.

A "gambler" will thus attempt to answer every question part. Many of his guesses will be wrong but the above strategy will give him a clear advantage over the "chickens". The more "certain correct" answers the "gambler" is able to write in before resorting to strategic marking, the more effective this system will be, since the probability predictions for the remaining blanks will increase in accuracy with increasing numbers of correct answers on which to base the predictions. The system favours the strong candidate and is of less value for the weak candidate. It is of no value at all if the candidate knows nothing. Clearly a good "chicken" will always beat a mediocre "gambler", but in border-line cases even a small improvement of two or three per cent obtained by strategic marking could make the difference between Fellowship and failure.

Sceptics can test the validity of this system by the following experiment: get a colleague to prepare a list of 60 five-part multiple choice questions, preferably obtained from previous F.R.C.R. papers, and a set of correct answers. Ask your colleague to fill in on a simulated answer sheet 150 correct answers selected at random from the 300 question parts. Let him then pass the answer sheet to you; *without looking at the questions*, fill in all the remaining blank answer spaces using the criteria described in the above system. Get your colleague to mark your final answer sheet. If the system works, your score will be significantly better than 150 out of 300 correct.

It may be thought that the foregoing is a facile treatment of a serious subject; it is certainly not meant to be so. What could be more serious than an expensive and stressful ordeal on which the future careers of the candidates depend? When success is at stake, surely a professional approach is not only acceptable but essential.

Yours, etc.,
P. J. ROBINSON.

Radiology Department,
St. James's Hospital,
Beckett Street,
Leeds 9.

(*Received December 1980*)

Ultrasonic measurement of the lumbar spinal canal

THE EDITOR—SIR,

We welcome the correspondence of Ottewell and Howells (1981) commenting on our recent letter on the subject of ultrasonic quantification of the lumbar spinal canal.

Without seeing full details of their proposals, we are not in the best position to discuss the details of their work. We shall await publication of their paper, referred to in their letter, with interest.

However, we are unsure about one point in their letter. They state that "each centre should adopt and rigidly adhere to its own scanning technique . . ." in order to ". . . establish its own set of normal values". If the normal range measured by one centre is significantly different from that achieved elsewhere, then this means, presumably, that the technique is subjective to a certain extent.

Our original letter was an attempt to initiate a debate on the value of this technique. Clearly such a debate has begun.

Yours etc.,
H. R. STOCKDALE,

Medical Physics Department,
City Hospital,
Nottingham NG5 1PG.

D. FINLAY.

X-ray Department,
Royal Infirmary,
Leicester.

(*Received March 1981*)

REFERENCE

OTTEWELL, D. and HOWELLS, P., 1981. The use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *54*, 430.

Book review

Medical Physics Handbooks.5. Thermoluminescence Dosimetry. By A. F. McKinley, pp. x+170, 1981 (Adam Hilger, Bristol) £11·95.
ISBN 0-85274-520-6

Thermoluminiscent dosimetry (TLD) now has an established place amongst radiological measuring techniques. It is essential therefore that any new physical scientist entering upon a career involving the measurement of ionizing radiation should be familiar with the theory and practice of TLD. This book provides an excellent introduction to the subject and its present state of development.

The first three chapters discuss luminescence phenomena, theoretical aspects of thermoluminescence, trapping and recombination models in lithium fluoride, supralinearity, phototransferred luminescence, and the thermoluminescence properties and dose measurement characteristics of a number of commonly used phosphors. Chapters 4 and 5 describe the use of TLDs for specific measurement applications including clinical, personal and environmental dosimetry and thermoluminescence dating. The last two chapters deal with practical problems and potential pitfalls in the use of TLDs including those associated with annealing, calibration and readout. An extensive list of references is provided.

The book is attractively produced and can be thoroughly recommended, not only to graduates but also to non-graduate technical staff working with TLD. I have only two very minor quibbles: 1 Gy is a rather high value to quote on p. 62 for the upper end of the range of skin doses found in diagnostic radiology, and the backscatter factor does not arise from backscattered electrons as stated on p. 145, but from backscattered photons.
J. L. HAYBITTLE.

1981, *British Journal of Radiology*, 54, 540–550

Proceedings of The British Medical Ultrasound Society

Abstracts of papers presented at the Twelfth Annual Meeting of the British Medical Ultrasound Society held at Portland Building, University Park, Nottingham, December 15 and 16, 1980

Cardiology

Chairman: F. G. M. Ross

Interventricular septal motion in hypertrophic cardiomyopathy (HCM) and simple septal hypertrophy (SSH), by J. Gehrke.
Fetal cardiac function and blood flow measurements by means of real-time and pulsed Doppler ultrasound, by J. S. McGhie and J. W. Wladimiroff.
Computer analysis of echocardiograms and synchronous apexcardiograms in relation to left ventricle function, by C. J. Martin and J. Weir.
Pattern analysis of echocardiograms, by L. M. Lewis.
The measurement of lateral resolution of phased array ultrasonic scanners and the effect of dynamic focusing, by M. J. Lunt, P. T. Gosling and S. J. Meldrum.

INTERVENTRICULAR SEPTAL MOTION IN HYPERTROPHIC CARDIOMYOPATHY (HCM) AND SIMPLE SEPTAL HYPERTROPHY (SSH)

By J. Gehrke

Department of Medicine, Division of Cardiovascular Disease, Clinical Cardiology, Royal Postgraduate Medical School, Hammersmith Hospital, London

There is still uncertainty among cardiologists whether to make the diagnosis of hypertrophic cardiomyopathy (HCM) or not, when a thick interventricular septum (IVS) is imaged during M-scanning (MS) or real-time B-scanning (RTBS), except when primary right heart disease is obvious. The tracings of MS and RTBS in 20 patients with secondary and ten patients with primary septal hypertrophy were reviewed to investigate septal behaviour and appearance during echocardiography.

The diagnoses of all 30 patients were proven by catherization and angiocardiography. In all patients showing an upper and mid-septal bulge, best seen during RTBS and in both groups, the IVS motion was directed towards the cardiac apex and only the lower part of the septum moved normally towards the left ventricular posterior wall. In some cases of secondary septal hypertrophy (SSH) the M-scan tracings showed a thick and immobile IVS, and all patients with a relatively small ventricle and a hyperkinetic apical contraction showed systolic anterior motion (SAM) of the subvalvular mitral valve apparatus in both groups.

It is concluded that a thick and immobile appearance of the IVS in MS or RTBS does not allow the diagnosis of hypertrophic cardiomyopathy to be made, since this feature may be seen in both groups of patients, with primary or HCM and secondary or simple septal hypertrophy. Even the presence of SAM is no further proof of HCM, since it signals chordal anterior motion in a small ventricle with hyperkinetic apical left ventricular wall (and not mitral valve motion, as shown earlier). It is suggested that the same patho-physiological mechanism may be responsible to move the upper and mid-septal bulge in both groups towards the cardiac apex, in order to prevent further narrowing of the left ventricular outflow tract during ventricular systole. Since a relative damping of myocardial structures is seen in both groups, malorientation of myocardial fibres may be the underlying pathology in both groups as well, enabling the particular patho-physiological mechanism of change in septal motion to set in. Other non-invasive features must therefore be developed to differentiate between hypertrophic cardiomyopathy and simple septal hypertrophy.

FETAL CARDIAC FUNCTION AND BLOOD FLOW MEASUREMENTS BY MEANS OF REAL-TIME AND PULSED DOPPLER ULTRASOUND

By J. S. McGhie and J. W. Wladimiroff

Department of Obstetrics and Gynaecology, Erasmus University, Rotterdam

Fetal cardiac geometry and function were determined from M-mode recordings and 2-D images. Particular emphasis is put on a new technique of measuring left ventricular cardiac output (LVCO) in normal subjects during the third trimester of pregnancy. LVCO values ranged between 100 and 260 ml per minute during the pregnancy period of 27–34 weeks and between 250 and 400 ml per minute during the period 34–41 weeks. A close correlation between LVCO and mean blood flow in the descending aorta was found ($P<0.01$). If it is assumed that combined right and left ventricular output is twice the LVCO, then 70–75% of the combined cardiac output is distributed to the descending aorta. Myocardial contraction force is revealed to be equal for both the longitudinal and transverse axis of the left ventricle and showed an increase with advancing gestational age.

COMPUTER ANALYSIS OF ECHOCARDIOGRAMS AND SYNCHRONOUS APEXCARDIOGRAMS IN RELATION TO LEFT VENTRICLE FUNCTION

By C. J. Martin and J. Weir

Department of Biomedical Physics and Bioengineering, University of Aberdeen, and Department of Diagnostic Radiology, Aberdeen Royal Infirmary

Computer analysis of echocardiogram traces showing movement of the left ventricle has become an accepted approach to the study of ventricle function. Apexcardiogram traces recorded simultaneously provide approximate indicators for the timing of pressure changes in the ventricle, and increase the amount of non-invasive information potentially available.

We have performed left ventricular studies using echocardiography and apexcardiography on more than 400 patients. These fall into three major groups (ischaemic heart disease, aortic valve disease and hypertrophic obstructive cardiomyopathy) and two minor groups (congestive cardiomyopathy and mitral valve disease). These have been compared with results from 50 normal subjects.

Ventricle dimension and rate of dimension change have been derived throughout the cycle from digitized echocardiogram traces. Pressure-volume loops for the ventricle have been constructed from ultrasonic and apexcardiographic data. Various parameters have been measured, and their value in diagnosis was discussed. In addition the beat to beat variability of several patients and volunteers has been studied to assess the accuracy of the method.

PATTERN ANALYSIS OF ECHOCARDIOGRAMS

By L. M. Lewis

Royal Postgraduate Medical School, Hammersmith, London

For many years now, ultrasound has proved valuable in the diagnosis of cardiological conditions, primarily by examination of the movements of valve cusps and chamber walls. The assessment has been largely by visual inspection of traces, although early, basic attempts at quantitation (such as measurement of the diastolic closure rate of valve cusps) indicated that much could be gained from a less qualitative approach.

An attempt is made here to analyze the motion of the following in a quantitatively rigorous manner: mitral valve leaflets; interventricular septum; left ventricular posterior wall; aortic root and valve. Data is taken from some 100 M-mode echocardiograms obtained during routine examination of patients with suspected mitral and/or aortic valve disease.

Tracings are digitized by Graf-pen system interfaced to a Hewlett-Packard HP2100A computer, data being normalized with respect to heart rate. The analysis procedure hinges upon correlation methods, which are presented in simple detail. Two features are extracted for each correlation study and plotted out on a feature diagram. Different disease types then cluster in different regions of the feature diagram, and with appropriate choice of features, the clustering is sufficiently close to allow differentiation between disease states.

A clear differential diagnosis may be made by this method for relatively blatant, uncomplicated situations like mitral stenosis, but the full potential of the technique will be seen with respect to less easily identified conditions. The extent to which this is already possible with the present approach is discussed. Some future hopes and present difficulties are also outlined.

THE MEASUREMENT OF LATERAL RESOLUTION OF PHASED ARRAY ULTRASONIC SCANNERS AND THE EFFECT OF DYNAMIC FOCUSING

By M. J. Lunt, P. T. Gosling and S. J. Meldrum

Department of Medical Electronics,
St. Bartholomew's Hospital, London

The lateral resolution of four phased array systems (Toshiba SSH-10A, EMI 4500, Kontron RT.400, Varian V.3000) was measured both in the scanning plane and across the plane by moving a point target until the echo fell to fixed fractions of the maximum. Measurements were made at three depths and at two angles. The machines without dynamic focusing (Toshiba, Kontron, Varian) all exhibited a poorer resolution in the scanning plane than across the plane. The EMI 4500 generally had similar resolutions in the two lateral directions, showing that the dynamic focusing improves the resolution. The resolutions were compared with those from a single crystal A-scan instrument (SKI Ekoline 20A) and an oscillating transducer system (SKI EkoSector 1).

The results indicate that phased array systems without dynamic focusing have poor resolution, but the inclusion of dynamic focusing can give resolutions similar to those achieved by geometric focusing alone.

Muscle imaging

Chairman: E. Barnett

An ultrasonic determination of cardiac muscle structures, by D. Nicholas, A. Nicholas and R. Greenbaum.
Ultrasonic tissue characterization of muscle, by E. Cady and J. Gardener.
Ultrasound imaging in the diagnosis of muscle disease, by J. Z. Heckmatt, V. Dubowitz and S. Leeman.

AN ULTRASONIC DETERMINATION OF CARDIAC MUSCLE STRUCTURES

By D. Nicholas, A. Nicholas and R. Greenbaum

Institute of Cancer Research, Sutton, Surrey,
Hammersmith Hospital, London, and
Cardiothoracic Institute, Brompton Hospital, London

We have developed techniques for investigating the structure of human soft tissues utilizing the diffractive nature of ultrasound scattering. Applying these techniques to tissues exhibiting a degree of isotropy, such as muscle fasciculi, allows the determination of both the orientation of the muscle structure and the macroscopic spacing of the fasciculi. Results are presented on an *in vitro* study of excised human hearts where special interest has been directed towards the wall of the left ventricle. Correlation of ultrasonic findings with histological examination of the tissues shows that diffraction analysis is capable of monitoring both the changes in muscle fibre orientation as a function of depth into the heart wall, and the macroscopic spacing of the aligned fibres at any specific depth.

Our techniques have been demonstrated to be applicable *in vivo* and apparatus is in existence which is capable of investigating patients suffering from cardiac diseases. It is thought that this technique may find an application in the estimation of the size of myocardial infarction and in conditions such as congestive cardiomyopathy and other ischaemic heart diseases.

ULTRASONIC TISSUE CHARACTERIZATION OF MUSCLE

By E. Cady and J. Gardener

Department of Medical Physics,
University College Hospital, London

A study is in progress using ultrasound for the quantitative characterization of normal and pathological muscle tissue. The research has been carried out using both volunteer patients and normal subjects. In order to make the technique easily applicable in the clinic we are using a single broad-band transducer and a modified commercial pulse echo imaging system. So as to determine the system independence of our work, several probes with similar characteristics have been used and tests have been performed to ensure that results obtained with them are readily comparable. RF echoes from a volume of tissue have been digitized and analyzed using both on and off-line computer systems. Methods of analysis include one-dimensional texture, amplitude statistics and correlation techniques.

As a result of the anisotropic nature of normal muscle tissue the various parameters have been measured as a function of the angle between the probe and the fasciculi (fibre bundles). For some pathologies, due to structural changes, this anisotropy is not found. In the normal subject several different muscle units in the leg, arm and back have been examined. Most of the pathological tissues have consisted of advanced dystrophic muscle and significantly different parameters have been obtained from these when compared with normals.

Our quantitative methods appear to have clinical potential both for the staging and monitoring of disease and for aiding early differential diagnosis. In order to achieve some of these aims work is being undertaken to develop a pattern recognition technique using both ultrasonic and conventional clinical tests.

ULTRASOUND IMAGING IN THE DIAGNOSIS OF MUSCLE DISEASE

By J. Z. Heckmatt, V. Dubowitz and S. Leeman

Department of Paediatrics and Neonatal Medicine,
Hammersmith Hospital, London

Diagnostic pulse echo ultrasound imaging has recently been described as a method of visualizing pathological change in dystrophic muscle. A study is now under way to establish the possible value of the technique as a diagnostic tool in muscle disorders of childhood.

A comparison has been made of the ultrasound appearance of the thigh muscles in 60 normal children, 13 with spinal muscular atrophy, 13 with progressive muscular dystrophy, and four with congenital muscular dystrophy. This latter disease, though showing dystrophic change in the muscle, is non-progressive. The children with spinal atrophy and muscular dystrophy were examined at the time of the diagnostic muscle biopsy. Transverse and longitudinal static B-scan ultrasound pictures of the thigh were obtained using a 5 MHz probe.

In normal children three anatomical landmarks—bone, fascia lata and the outer boundary of vastus intermedius—were always clearly seen. In the children with dystrophy and spinal atrophy the ultrasound appearances were altered. In both, increased echo from within the muscle atrophy was sometimes striking.

As a diagnostic screening tool, ultrasound is of less value than the serum CPK in the early diagnosis of the progressive forms of dystrophy. Ultrasound is potentially of greater value in the diagnosis of spinal muscular atrophy and congenital muscular dystrophy.

Upper abdominal examinations

Chairman: E. Barnett

Intrarenal anatomy: techniques and significant measurements. The cortico-pyramidal ratio, by W. R. Lees.
The use of an anthropomorphic ultrasound phantom, by R. E. A. Dye.
The clinical value and limitation of liver ultrasound for the detection of metastases, by H. B. Meire and P. Farrant.
Ultrasonic identification of vertebral levels in the abdomen and the clinical implications, by S. J. Pussell and D. O. Cosgrove.
Anomalies of the hepatic artery—an ultrasonic study, by M. C. Bossi, D. O. Cosgrove and S. J. Pussell.

INTRARENAL ANATOMY: TECHNIQUES AND SIGNIFICANT MEASUREMENTS. THE CORTICO-PYRAMIDAL RATIO

By W. R. Lees

The Middlesex Hospital, London

A systematic approach to scanning technique is essential to reproducibly assess the components of intrarenal anatomy.

The major and minor axes must first be determined and measured, and their orientation assessed. Renal orientation varies considerably with position, and hence scanning in the coronal, horizontal and parasagittal planes in the supine, prone and lateral positions is best done with real-time. The static scanner is then used in predetermined planes for high resolution studies.

The echo amplitudes and relative sizes of cortex, medullae and sinus must be assessed with a standard technique. The ideal way is to scan in the plane of the two major axes (filleting the kidney) and at right angles to these.

The cortex and medullae are optimally visualized when the beam impinges normal to the renal capsule and parallel to the long axis of the pyramid. Given a full bladder the related minor calyx will be seen. In this projection the arcuate artery defines the cortico-pyramidal junction. Thus, pyramidal height and cortical thickness can be anatomically assessed, using the renal capsule, arcuate artery and calyx as benchmarks. The cortico-pyramidal ratio (mean 1·5) when calculated may prove useful in the evaluation of renal parenchymal disease.

The use of real-time and static scanning in evaluating renal vessels and their patency was illustrated.

THE USE OF AN ANTHROPOMORPHIC ULTRASOUND PHANTOM

By R. E. A. Dye

Regional Radiation Physics and Protection Service,
Queen Elizabeth Medical Centre, Birmingham

An anthropomorphic ultrasound system has been constructed representing a longitudinal section through the human liver, including the diaphragm, kidney and gall bladder, with simulated ducts, cysts and gall-stones. The images obtained are extremely realistic and can illustrate important aspects of the imaging process which can be of great clinical interest.

The phantom has been used to complement the AIUM-type wire phantom for quality assurance on ultrasonic equipment, and has been used to great effect for teaching purposes of technical aspects of the instrumentation and of scanning techniques. The phantom has proved very valuable as a standard test object for a simulated-clinical inter-comparison between various systems in the West Midlands Regional Health Authority.

THE CLINICAL VALUE AND LIMITATION OF LIVER ULTRASOUND FOR THE DETECTION OF METASTASES

By H. B. Meire and P. Farrant

Department of Radiology, Clinical Research Centre, Harrow, Middlesex

An investigation has been performed to attempt to assess the clinical value of ultrasound examination for the detection or exclusion of hepatic metastases in patients with known primary carcinoma of the breast or colon.

In 201 patients with primary breast carcinoma initial liver ultrasound examination did not change the clinical staging. Eight of these patients subsequently developed liver metastases whilst undergoing ultrasound surveillance. In five patients ultrasound detected the metastases before clinical or biochemical evidence was obtained and in three patients the liver function tests were abnormal before ultrasound evidence of metastases was detected. In none of these eight patients did the finding of the metastases significantly alter patient management or outcome.

In 145 patients with primary bowel carcinoma ultrasound examination revealed the presence of metastases in 22% of patients. Metastases were more common in patients with carcinoma of the stomach and proximal colon and were least common from carcinoma of the rectum. The ultrasound detection of metastases in patients with primary bowel carcinoma significantly influenced patient management.

The clinical value of ultrasound for the detection of liver metastases is dependent upon the site of the primary malignancy.

ULTRASONIC IDENTIFICATION OF VERTEBRAL LEVELS IN THE ABDOMEN AND THE CLINICAL IMPLICATIONS

By S. J. Pussell and D. O. Cosgrove

Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey

The exact localization of structures within the abdomen depends on defining the relationship with surface markers or with normal nearby organs or vessels. This lack of bony reference points can lead to difficulties in siting lesions with respect to other radiological imaging techniques and also in following abnormalities on serial studies.

In oncology it is particularly problematic that masses in the para aortic region that are well defined on ultrasound cannot be related by bone structures for incorporation into radiotherapy planning. Also, the same area of the abdomen needs to be adequately screened on repeated studies when tumour masses shrink in response to chemotherapy. In general, it is often helpful to accurately interrelate the various complementary imaging methods, for example abdominal aortic aneurysms well demonstrated by ultrasound can be compared with plain films, IVUs and angiograms.

It is possible to identify vertebral levels in almost all patients when the aorta can be visualized. Disc spaces appear as a slightly convex surface on the spine that allows penetration of sound to the spinal canal whereas vertebral bodies are slightly concave and totally reflect the beam. By counting up and down all vertebral bodies and discs can be identified and structures can be related to them.

Examples of ultrasound scans of normal anatomy and of pathology were presented to demonstrate the technique for identifying vertebral levels. Radiological confirmation was given to show the accuracy of the method.

ANOMALIES OF THE HEPATIC ARTERY—AN ULTRASONIC STUDY

By M. C. Bossi, D. O. Cosgrove and S. J. Pussell

Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey

Variations in the origin and course of the hepatic artery (HA) are so often encountered that the so-called "normal pattern" is actually uncommon. Clinically important variations include the anomalous origin of the hepatic artery from the superior mesenteric artery (SMA) instead of the coeliac axis where it may be at risk in duodenal surgery. Within the porta the right hepatic artery branch (RHA) usually passes posterior to the common hepatic duct; when it lies anterior it is at risk in gall bladder surgery.

Ultrasound was used to assess the frequency with which these variations could be detected. The origin from the SMA was characterized on longitudinal sections to the right of the aorta by the HA, here seen in cross section, lying posterior to the splenic vein instead of supero-anterior. The anomalous anterior RHA within the porta was readily located on oblique views along the common hepatic duct. The artery, seen here in cross section, normally lies between the duct and the right portal vein branch; in the anomaly it lies anterior.

In 50 cases in which good views of the relevant anatomy were possible the origin of the hepatic artery could not be visualized in 16% and the RHA in the porta in 20%. In the remainder an anomalous origin from the SMA was found in 4% and an anterior RHA in 6%. These results correspond closely with those reported in the anatomical literature. Further cases were presented.

Ultrasound can be useful to alert the surgeon to these common variations before duodenal and gall bladder surgery.

Orthopaedics and rheumatology

Chairman: D. H. Trapnell

Measurement of the spinal canal, by R. W. Porter.
The value of sonography for evaluation of patients with clinically suspected spinal stenosis, by M. Asztely, R. Kadziolka, K. Hanai, T. Hansson and A. Nachemson.
An examination of the role of diagnostic ultrasound in the assessment of the lumbar spinal canal dimension, by H. R. Stockdale, D. Finlay and E. Lewin.
Ultrasonic measurement of the lumbar spinal canal: physical validity, by D. Ottewell and P. Howells.
Evaluation of popliteal cysts and painful calves with ultrasonography: comparison with arthrography, by B. M. Gompels and L. G. Darlington.
Baker's cysts and thrombophlebitis, by F. G. Simpson, P. J. Robinson, M. Bark and M. S. Losowsky.

MEASUREMENT OF THE SPINAL CANAL

By R. W. Porter

Department of Orthopaedics, Doncaster Royal Infirmary, Doncaster

Measurements of the spinal canal have been obtained by ultrasound using a Nuclear Enterprises Diasonograph 4200 from over 2000 volunteer subjects and a similar number of patients with back and/or leg pain. The mean intraobserver error for 22 patients and the interobserver error for 56 patients was less than half a millimetre. The measurements are generally widest at L1, narrowing towards L4, and widening again at L5. The canal is surprisingly large in children; it reaches its maximum diameter in late teens, gradually reducing by about a millimetre in later life. We have not been able to show any difference in the measurements of heavy manual and sedentary workers. Patients attending hospital with back pain tend to have narrower canals than the rest of the population. Fifty-six percent of patients with lower lumbar disc lesions, and 70% of patients with neurogenic claudication were below the tenth percentile.

Ultrasound measurements of the canal are proving a useful routine investigation for patients attending a back pain clinic. Like the plain X-ray, it must be interpreted in the light of the history and examination, but an appreciation of available space that can be compromised by the precipitating lesion, assists the diagnosis. The concept of space in the canal is understood and appreciated by the patient. It may help him to accept a chronic problem rather than seek an impossible cure. The shape as well as the size of the spinal canal varies considerably within the population. The small trefoil shape canal at L5 is a dangerous combination because the nerve roots are vulnerable to compression in the presence of a disc lesion, degenerative change or unnatural segmental movement. The trefoil shape can be suspected when the ultrasound measurements at L5 are less than L4, whilst the majority of patients have triangular or dome-shaped canals at L5 with measurements wider than at L4.

Vertebral displacement in spondylolisthesis can often be identified by ultrasound. The narrow canal is especially important in the symptomatology of degenerative spondylolisthesis. Ultrasound measurement of the canal will confirm the diagnosis of neurogenic claudication which has been first suspected on clinical grounds. Myelography is unnecessary for the many patients who are prepared to accept their claudication symptoms and live within their limitations. Spinal surgery is sufficiently complex to make a pre-operative measurement of the canal worthwhile routinely. It will influence the surgeon in the choice of operation and its extent.

THE VALUE OF SONOGRAPHY FOR EVALUATION OF PATIENTS WITH CLINICALLY SUSPECTED SPINAL STENOSIS

By M. Asztely, R. Kadziolka, K. Hanai, T. Hansson and A. Nachemson

Departments of Orthopaedic Surgery and Diagnostic Radiology, Sahlgren Hospital, Göteborg, Sweden

A new approach for depiction of the lumbar spinal canal was introduced by Porter *et al.* in 1978. Ultrasonic grey-scale B-scanning was used and the width of the spinal canal was measured from the displayed echoes. An initial investigation was undertaken to clarify the structural origin of the recorded echoes and to determine the precision of the measurements. Ten fresh lumbar spine segments were measured by a static ultrasound scanner using a 2·25 MHz transducer. Having established the usefulness of the technique, we used it to investigate patients with clinically suspected spinal stenosis. The current method of evaluating such patients is lumbar myelography with positive contrast. The relation between measurements made on myelography films would show the value of ultrasound for diagnosis of spinal stenosis. Twenty patients were examined with myelography and with sonography according to the method described by Porter. Forty-five measurements were obtained. There was a correlation between the shortest ventrodorsal distance at the levels of the intervertebral spaces on myelography films and the corresponding measurement with sonography. A distance obtained with sonography of more than 14 mm excludes spinal stenosis according to criteria used when evaluating myelograms.

AN EXAMINATION OF THE ROLE OF DIAGNOSTIC ULTRASOUND IN THE ASSESSMENT OF THE LUMBAR SPINAL CANAL DIMENSION

By H. R. Stockdale, D. Finlay and E. Lewin

Medical Physics Department, City Hospital, and X-ray Department, University Hospital, Nottingham

The use of diagnostic ultrasound to assess spinal canal dimensions is discussed. In particular, the inability to obtain reliable and reproducible results in the *in vivo* situation is noted. In view of this uncertainty, a series of experiments using dried lumbar vertebrae in a water bath was carried out in order to correlate the dimensions recorded on the A-scan with the anatomical bony structures. The results indicate that diagnostic ultrasound can be used to obtain a measure of the canal size in this *in vitro* situation. However, we feel that the extension of this conclusion to the *in vivo* clinical situation is fraught with problems. These are reliable echo identification and problems associated with location of the calipers. As a consequence we must express strong reservations on the proposed use of this technique at the present in individual patient management.

ULTRASONIC MEASUREMENT OF THE LUMBAR SPINAL CANAL: PHYSICAL VALIDITY

By D. Ottewell and P. Howells

Bioengineering Research Unit, Doncaster Royal Infirmary, Doncaster

Ultrasonic measurement of the lumbar spinal canal was first described in 1978, and has been the subject of some controversy particularly with respect to the clinical relevance, accuracy and reproducibility of the measurements made. The clinical significance of these measurements has been discussed elsewhere, but up to the present time no attempt has been made to examine the physical processes giving rise to the observed echo patterns.

This paper examines the physical interactions of low power ultrasonic energy with some of the internal structures of the spine. The mechanisms by which this energy may be reflected by the vertebral lamina and the posterior wall of the vertebral body are discussed, and the concept of the so-called "acoustic window" is shown to be inadequate. An alternative theory is proposed, supported by experimental evidence, which predicts echo amplitudes consistent with those observed under clinical conditions. The reproducibility and accuracy of *in vivo* measurements is discussed in the light of this theory. The principle of using diagnostic ultrasound to assess the size of the lumbar spinal canal is validated, but subject to more stringent operational control than was originally inferred.

EVALUATION OF POPLITEAL CYSTS AND PAINFUL CALVES WITH ULTRASONOGRAPHY: COMPARISON WITH ARTHROGRAPHY

By B. M. Gompels and L. G. Darlington

Radiology Department and Rheumatology Unit, Epsom District Hospital, Epsom, Surrey

Grey-scale ultrasonography will detect reliably the presence of clinically significant popliteal cysts and of fluid collections which do not fill on arthrography. Use of a 5 MHz transducer enables ultrasound to demonstrate acute rupture of cysts and soft tissue changes resulting from recent leaks.

Evidence of rupture has been demonstrated by ultrasound in eight patients; free fluid was shown in four patients and soft tissue changes characteristic of recent leakage were apparent in the remaining four patients.

In a further study, ultrasonography demonstrated popliteal cysts with a prevalence of 31% (22/72) in 36 patients with definite or classical rheumatoid arthritis compared with 4% (3/72) in controls closely matched for age and sex. This difference in prevalence between the rheumatoid patients and controls was highly significant.

Ultrasonography may further assist in quantitative, sequential assessment of patients with painful knees and calves.

BAKER'S CYSTS AND THROMBOPHLEBITIS

By F. G. Simpson, P. J. Robinson, M. Bark and M. S. Losowsky

Department of Medicine, St. James's Hospital, Leeds

The mimicking of deep vein thrombosis of the lower limb by a popliteal or Baker's cyst has been recognized for over a century. Recently this event has been found to be fairly common in patients with severe arthritis and termed the pseudo-thrombophlebitis syndrome. We have studied prospectively 43 non-surgical patients presenting with unilateral calf pain or swelling by arthrography, venography and ultrasonography. Only 14 (33%) of patients had venographic evidence of DVT. Five of these patients also had popliteal cysts which in four cases probably contributed to symptoms. Eleven patients (25%) had popliteal cysts and normal venograms and nine of these were felt to be the cause of the symptoms. Eighteen patients had normal venograms and arthrograms. No physical sign or combination of signs distinguished between the different diagnostic groups. Ultrasound examination of the popliteal fossa using a 2.5 MHz transducer detected only two of the 16 popliteal cysts with no false positives. This contrasts with other workers' findings. However, the vast majority of patients in other series had arthritis (usually inflammatory) compared to only eight (50%) of our patients with Baker's cysts, and the Baker's cysts in previous studies were generally diagnosed clinically. It seems likely that this difference in patient selection accounts for the discrepancy. In any case the relative frequency with which Baker's cyst and DVT co-exist means that venography should be performed even if a Baker's cyst is demonstrated.

Obstetrics

Chairman: P. Davies

Ultrasonic estimation of uterine size in gestational trophoblastic tumours (GTT), by J. E. Boultbee and R. H. J. Begent.
The psychological effects on the mother of real-time ultrasound in antenatal clinics, by A. E. Reading, C. M. Sledmere, S. Campbell, R. Mooney, D. Cox, P. Chudleigh, J. Beedle and H. Ruddick.
Ultrasound visualization of intrauterine haematomata in threatened abortion, by M. Mantoni and J. F. Pedersen.
Ultrasound evidence of sexual difference in fetal size in first trimester, by J. F. Pedersen.

ULTRASONIC ESTIMATION OF UTERINE SIZE IN GESTATIONAL TROPHOBLASTIC TUMOURS (GTT)

By J. E. Boultbee and R. H. J. Begent

Departments of Radiology and Medical Oncology, Charing Cross Hospital, London

Ultrasound has been used to assess the volume of the uterus in 30 patients with GTT. The patients were a group requiring cytotoxic chemotherapy after evacuation of hydatidiform mole or for choriocarcinoma. The relationship between uterine volume and Human Chorionic Gonadotrophin (HCG) was compared.

Forty-eight per cent of patients had a uterine volume over 150 cc and HCG was above 800 mIU/ml in all of these. In a further 36%, however, where HCG level was over 800 mIU/ml the uterine volume was considered within normal limits being under 150 cc.

The ratio between the uterine volume and the serum HCG levels varies considerably. The finding of a normal sized uterus cannot be taken to imply the absence of a gestational trophoblastic tumour in the uterus. Uterine enlargement in the presence of HCG however is nearly always indicative of active uterine disease. The ultrasonic appearances and the use of ultrasound to monitor size change were described in this disease.

THE PSYCHOLOGICAL EFFECTS ON THE MOTHER OF REAL-TIME ULTRASOUND IN ANTENATAL CLINICS

By A. E. Reading, C. M. Sledmere, S. Campbell, R. Mooney, D. Cox, P. Chudleigh, J. Beedle and H. Ruddick

Department of Obstetrics and Gynaecology, King's College Hospital Medical School, London

While the diagnostic benefits of ultrasound in obstetrics are well documented, less attention has been given to the psychological impact of scanning. With the development of small and portable real-time scanners, the possibility emerges of employing routine screening of the whole antenatal population for certain fetal abnormalities, as well as assisting in accurately defining fetal age. A study is presented which has evaluated the psychological and behavioural effects of receiving high definition pictures of the moving fetus within the first trimester of pregnancy. This paper focuses on the short term effects of real-time scans in terms of attitudes towards the fetus and being pregnant, along with the acceptability and subjective reactions towards the scanning procedure itself. A consecutive series of primiparous women were randomly allocated to one of two ultrasound conditions defined by the level of feedback, at antenatal booking clinics; high feedback condition in which women had access to the monitor and verbal feedback was linked to fetal activity that was visible ($n=67$); low feedback in which the monitor's screen was not visible and only a global evaluation of progress was provided ($n=62$). In the high feedback condition the scan was prolonged until movement was discernible. The results demonstrated the powerful effects of the scan on attitudes towards being pregnant and the fetus. The groups differed in terms of their attitudes towards the scanning procedure and their emotional state at the time of the scan. The implications of these findings are discussed in terms of studying "at risk" mothers, along with the rationale for enhancing feedback at this stage, which may anticipate and augment the awareness that comes about later in pregnancy with the maternal perception of fetal movement.

ULTRASOUND VISUALIZATION OF INTRAUTERINE HAEMATOMATA IN THREATENED ABORTION

By M. Mantoni and J. F. Pedersen

Ultrasound Laboratory, Glostrup Hospital, Glostrup, Denmark

Ultrasonic scanning in patients with symptoms of threatened abortion occasionally revealed an echo-free area between the membranes and the uterine wall. The echo-free area was found in patients who had a live fetus of an age of 11–20 weeks and is believed to represent blood. Seven smaller haematomata of less than 35 ml gradually disappeared and the pregnancies continued until term. Three patients who had haematomata of more than 50 ml subsequently aborted or had a premature delivery.

ULTRASOUND EVIDENCE OF SEXUAL DIFFERENCE IN FETAL SIZE IN FIRST TRIMESTER

By J. F. Pedersen

Ultrasound Laboratory, Glostrup Hospital, Glostrup, Denmark

In order to establish a local normal series of fetal growth, 101 normal pregnancies were studied by ultrasonic scanning. In weeks 7 to 13 the fetal crown–rump length (CRL) was measured 2–4 times at bi-weekly intervals. From week 12 until term the biparietal diameter (BPD) was determined every four weeks. The CRL and BPD were on average 2·0 mm bigger in male fetuses than in female ones. The unexpected sex difference in fetal size already in the first trimester suggests a genetic rather than a hormonal mechanism behind this phenomenon.

Tissue characterization

Chairman: T. A. Whittingham

Evidence for ultrasonically induced cavitation *in vivo*, by G. R. ter Haar, S. Daniels and C. R. Hill.
Real-time machine to perform *in vivo* angular diffraction measurements, by D. Nicholas, D. O. Cosgrove and S. Pussell.
The effect of tissue movement on *in vivo* ultrasonic tissue characterization, by L. M. Eastwood, A. N. R. Law and A. P. Bayliss.
The clinical value of placental tissue characterization using digital techniques, by D. C. Almond, D. W. Fenton, A. Kennedy and W. I. J. Pryce.
Discriminant analysis applied to the ultrasonic characterization of diffuse liver disease, by R. A. Lerski, M. J. Smith, P. Morley, E. Barnett, R. N. M. MacSween, P. R. Mills and G. Watkinson.
Clinical application of *in vivo* tissue characterization, by D. O. Cosgrove, M. C. Bossi, P. Garbutt, D. Nassiri, D. Nicholas, S. J. Pussell, A. Scott-Malden, C. R. Hill and V. R. McCready.

EVIDENCE FOR ULTRASONICALLY INDUCED CAVITATION *IN VIVO*

By G. R. ter Haar, S. Daniels and C. R. Hill

Physics Division, Institute of Cancer Research, Sutton, Surrey, and Pharmacology Department, Oxford University

There is ample evidence that cavitation may play an important role in producing biological effects when samples are irradiated with ultrasound *in vitro*. There is some debate as to whether cavitation can occur in intact mammalian tissues *in vivo*. Evidence for *in vivo* bubble activity to date comes largely from histological studies and observation of localized damage using an electron microscope.

This paper describes a technique by which bubble formation in the hind legs of guinea pigs during ultrasonic irradiation (0.125–1.0 Wcm^{-2} spatial average intensity) may be observed.

The detection system, developed to study the formation of decompression bubbles in deep sea divers, consists of a modified 8 MHz Kretz mechanical sector scanner which produces bistable ultrasonic B-scan images. The gain of the system is set so that only echoes arising from reflections at the skin line, bone and gas interfaces are displayed. The equipment has been used extensively to study the development of bends in experimental animals.

Experiments have been carried out to study the formation of cavities as a result of therapeutic ultrasound. The source of therapeutic ultrasound is a Rank Sonacel Multiphon^{C} operating at 3 MHz and 0.75 MHz, and at spatial average intensities in the range 0.125–1.0 Wcm^{-2}.

Bubbles are seen to appear in subcutaneous fat, in fascia associated with muscle, and at higher intensities, in muscle. Time course analysis of the patterns indicate that both intra- and extravascular cavities are found. Application of external pressure decreases the number of bubbles detected.

A REAL-TIME MACHINE TO PERFORM *IN VIVO* ANGULAR DIFFRACTION MEASUREMENTS

By D. Nicholas, D. O. Cosgrove and S. Pussell

Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey

A rigorous *in vivo* characterization of tissue pathologies has previously been reported which utilizes the diffractive scattering of ultrasound by human soft tissues. Such an approach is based upon the structural configuration of the acoustic scatterers present in tissue, which is indicative of the pathological condition of the tissue.

These recent reports also indicated that the scattering of ultrasound from small tissue volumes was dependent upon both the orientation of the tissue volume and any movements with time. Indeed, it was shown that the tissue movements complicated some of the diffraction measurements to such an extent that the results could not be interpreted. This has prompted us to perform the diffraction measurements over a very short time interval (less than 40 μs) to eliminate any movement from the measurements.

A phased-array real-time scanner has been adapted to perform a form of diffraction scanning across the elements of its array. Operating at 2.5 MHz this prototype machine displays the signal intensity scattered from a selected region of tissue as recorded by each of the 21 receive elements of the array. The tissue volume interrogated is defined by the transmit beam width and pulse length at that position.

A description of this novel angular diffraction technique was given together with the results from a pilot study of 60 patients, where its ease of use has proved its clinical acceptance.

THE EFFECT OF TISSUE MOVEMENT ON *IN VIVO* ULTRASONIC TISSUE CHARACTERIZATION

By L. M. Eastwood, A. N. R. Law and A. P. Bayliss

Departments of Bio-Medical Physics and Bio-Engineering, and Radiology, University of Aberdeen

Computer analysis of signals due to ultrasound backscattered from tissue can contribute significantly to tissue identification. Signal features closely related to the autocorrelation function have been shown to be particularly useful in distinguishing between fresh, normal, *in vitro* tissues. In applying these techniques to clinical tissue characterization, tissue motion may affect results. An instantaneous record may not be a good estimate of average tissue properties. If tissue motion is purely translational, then a sample at one instant is as valid as that at any other. If, however, compressive motion occurs in response to, say, blood pressure changes, then it may help to record at various stages in the cardiac cycle, to obtain an "average property" estimate, or to record always at the same point in the cardiac cycle to standardize results.

In order to investigate this problem, the authors have developed a system to record backscatter signals at various stages of the cardiac cycle. A microprocessor is interfaced to an Emisonic 4200 scanner, an ECG amplifier, and a digital cassette recorder. Results of a study of the importance of tissue motion in characterizing abdominal tissues were presented.

THE CLINICAL VALUE OF PLACENTAL TISSUE CHARACTERIZATION USING DIGITAL TECHNIQUES

By D. C. Almond, D. W. Fenton, A. Kennedy and W. I. J. Pryce

Departments of Medical Physics and Clinical Engineering, Obstetrics and Gynaecology, and Pathology, Northern General Hospital, Sheffield

Premature aging of the placenta, which can be seen on the ultrasonic B-scan as diffuse textural changes, has been correlated with small-for-dates babies, so monitoring of placental ultrasonic appearance could prove clinically useful.

A series of antenatal patients has been scanned and the digitized video waveform from the placental tissue has been recorded and analysed. Statistical parameters derived from this data correlate with textural features of the B-scan image, so a comprehensive study of the placental ageing process is now possible using quantitative indices of placental texture.

The statistical and texture analysis parameters describing the B-scan image have been used to monitor placental ageing in a group of antenatal patients. A brief description of the data collection system and analysis techniques were presented together with the results. The clinical value of this pilot study was assessed with reference to the progress of pregnancy and pathological investigation of the post partum placenta.

DISCRIMINANT ANALYSIS APPLIED TO THE ULTRASONIC CHARACTERIZATION OF DIFFUSE LIVER DISEASE

By R. A. Lerski and M. J. Smith

Department of Clinical Physics and Bio-Engineering, West of Scotland Health Boards, Glasgow

P. Morley, E. Barnett and R. N. M. MacSween

Western Infirmary, Glasgow

P. R. Mills and G. Watkinson

Gartnavel General Hospital, Glasgow

Previously reported work by our group has shown that the use of texture analysis on digitally recorded ultrasonic signals can provide diagnostically useful data in diffuse liver disease. The technique has been extended through the use of new "texture" measures and a rigorous multivariate analysis applied to design optimal discriminant functions able to distinguish normal from diffusely abnormal liver with an accuracy greater than 90% in a group of more than 100 cases. This is considerably in excess of the accuracy achievable by the radiologist with standard grey-scale B-scanning both in our own and other reported experience.

The extent to which it has proved possible to differentiate between the varying disease stages of alcoholic liver disease was also discussed.

CLINICAL APPLICATION OF *IN VIVO* TISSUE CHARACTERIZATION

By D. O. Cosgrove, M. C. Bossi, P. Garbutt, D. Nassiri, D. Nicholas, S. J. Pussell, A. Scott-Malden, C. R. Hill and V. R. McCready

Royal Marsden Hospital and Institute of Cancer Research Sutton, Surrey

In vivo tissue characterization obtained with conventional B-scanners enables quantitation of echo intensity properties of tissue irradiated with ultrasound. To be of practical clinical use the quantitation method for tissue characterization should be simple and quick to operate. We have developed a system for collecting data directly off the analogue scan convertor memory of a B-scanner and storing this on a digital cassette tape system. Data to be stored is analysed into 8 bits. Two image sizes can be handled, a 12 cm^2 region of 256 × 256 pixels for large portions of the scan and a 3 cm^2 area of 64 × 64 pixels that can be positioned over a region of interest and takes only 15 s to collect. The buffer tape store can be left unobtrusively by the scanner so that data can be collected during normal diagnostic scanning sessions and analysis carried out later.

This method has been applied to patients with liver disease, both diffuse and malignant. Those patients with diffuse liver disease proved by biopsy were compared with normal subjects to attempt to establish normal parameters and to distinguish various types of liver histologies, *e.g.* cirrhosis, fatty change, hepatitis. Those with malignant livers were studied to attempt to categorize the range of appearances in the liver of tumour associated with malignancies in the GIT, lung, breast, ovary, lymphatic system.

The preliminary results from these studies were presented.

Blood flow

Chairman: D. O. Cosgrove

Doppler spectra conditioning and its benefits in Doppler flowmetry, by V. C. Roberts and A. J. Sainz.
Transcutaneous blood flow measurement—the problems and a solution, by P. J. Fish.
Ultrasonic investigations of the carotid artery, by J. P. Woodcock, R. Skidmore, R. Lusby, W. Jeans and R. Baird.

DOPPLER SPECTRA CONDITIONING AND ITS BENEFITS IN DOPPLER FLOWMETRY

By V. C. Roberts and A. J. Sainz

Department of Biomedical Engineering, King's College Hospital Medical School, London

In the last 15 years ultrasound has become a major tool in the investigation, in humans, of the cardio- and peripheral vascular systems. In particular, with the use of the Doppler effect, great advances have been made in the study of circulatory haemodynamics, including the possibility of vessel visualization.

This paper presents an add-on circuit which can be used to provide clearer Doppler signals in high noise environments. The use of such a system has the obvious result of enabling better interpretations to be made of haemodynamic parameters like peak and mean velocity. Use of the system in conjunction with more recently developed vessel visualization instruments which use Doppler techniques, because of the enhanced signal to noise ratios, leads to the production of better and more defined images.

The proposed electronic instrumentation is easily adaptable to any directional CW or pulsed Doppler velocimeter because it only processes Doppler shift spectra in the audio frequency range. It has the added advantage that it can be implemented with readily available electronic components.

TRANSCUTANEOUS BLOOD FLOW MEASUREMENT—THE PROBLEMS AND A SOLUTION

By P. J. Fish

Radiology Department, Clinical Research Centre, Harrow, Middlesex

The methods of transcutaneous blood flow measurement in general fall into two camps. They are flow measurement via uniform insonation of the blood vessel and via measurement of the velocity profile. The first method requires separation of the vessel of interest from the other interfering vessels and is limited in its area of deep vessels. The measurement via the velocity profile for the use in larger vessels is potentially achievable using a pulsed Doppler instrument.

An instrument (MAVIS) which overcomes some of the problems associated with this method of flow measurement has been developed and has the following features.

1. Doppler frequency measurement in the presence of noise is made using a noise subtraction technique.
2. Doppler images of the vessel aid the operator in beam location and maintenance.
3. A method of angle measurement requiring two cross-sectional scans of the vessel for vessel-axis orientation measurement is used.
4. A correction is made for the effect of the low frequency Doppler cut-off taking into account the velocity profile shape.
5. The effect of the finite length and width of the pulsed Doppler sampling volume on the measured velocity profile and flow rate are computed taking into account the velocity shape, variation of the sample volume width along the beam/vessel orientation.

The results of *in vitro* tests confirm that the flow measurements made are accurate and substantially independent of vessel depth, size and beam/vessel angle.

Measurements made on volunteers and patients have shown good reproducibility of flow measurements and the instrument's use in assessing the haemodynamic effect of arterial lesions.

ULTRASONIC INVESTIGATIONS OF THE CAROTID ARTERY

By J. P. Woodcock, R. Skidmore, R. Lusby, W. Jeans and R. Baird

Bristol Royal Infirmary, Bristol

Transient or permanent stroke is commonly associated with atherosclerotic lesions of the extracranial arteries. Ultrasonic techniques now play an important part in the clinical management of these patients. In a study involving approximately 60 carotid arteries from patients with transient ischaemic attacks, we have investigated the use of a pulsed Doppler imaging system (MAVIS), a real-time ultrasound scanner with an attached pulsed Dopper (ATL), and periorbital investigations using a continuous wave Doppler flowmeter. These results have been compared with contrast angiograms of the carotid arteries, and operative findings. The indirect periorbital tests satisfactorily detect lesions of greater than 50% diameter stenosis and both imaging systems reliably demonstrate lesions shown arteriographically to be greater than 20% diameter reduction. The adventages and disadvantages of both types of imaging system were discussed and recommendations made which should improve the level of correct diagnosis.

Breast imaging

Chairman: D. O. Cosgrove

Ultrasonic Doppler studies of the breast, by P. N. Burns, M. Halliwell, P. N. T. Wells and A. J. Webb.
Mirror axicons for improved ultrasonic imaging, by J. C. Bamber, R. L. Clarke, C. R. Hill and P. F. Wankling.
Early detection of breast cancer: the value of ultrasound mammography, by B. J. Hackeloer, G. Lauth, B. Huneke, V. Duda and R. Buchholz.
Ultrasound examination of the breast, by J. T. Ennis and M. Reilly.

ULTRASONIC DOPPLER STUDIES OF THE BREAST

By P. N. Burns, M. Halliwell, P. N. T. Wells and A. J. Webb

Department of Medical Physics, Bristol General Hospital and Department of Surgery, Bristol Royal Infirmary

The vascularization associated with the metabolism of malignant breast tumours gives rise to characteristic Doppler blood-flow signals. These signals differ qualitatively from those associated with benign lesions and allow malignant lesions to be identified with a sensitivity of at least 75%. Several descriptors of these Doppler signals have been tested, including those derived from the maximum frequency envelope and the Doppler power spectrum. Best separation between benign and malignant lesions is obtained by comparing signals from suspect and contralateral sites on a given individual. Corresponding main arterial sites in normal breast pairs are sufficiently symmetrical to allow this. Consideration of the frequency spectra and the powers of Doppler signals leads to the rejection of models of tumour vascularization in which Doppler signals arise from capillary perfusion or from a single feed artery. The data are compatible with a multiple feed artery model, and this is supported by evidence from contrast angiography.

MIRROR AXICONS FOR IMPROVED ULTRASONIC IMAGING

By J. C. Bamber, R. L. Clarke, C. R. Hill and P. F. Wankling

Institute of Cancer Research, Royal Marsden Hospital, Clifton Avenue, Sutton, Surrey

The maximum lateral resolution obtainable in pulse-echo imaging, using conventionally focused transducers, is limited by a compromise with the depth over which this resolution is maintained. Various methods proposed to circumvent this problem have included the use of multiple transducers focused strongly to cover different depth zones, phased arrays for focal scanning, and axicon or cylindrical sources for projecting a line focus into the patient. This paper describes studies of mirror axicon systems, designed with the aid of a computer ray-plotting programme, which are used in conjunction with conventional transducers. These devices transmit a conical acoustic wave, which tends to converge towards a line focus, and have a similar directivity pattern for their sensitivity as receivers. Tests in imaging phantoms and the female breast suggest that wide-aperture pulse-echo axicons offer considerable potential for producing high resolution images which possess a large depth of focus. For example, at 4 MHz a measured 3 dB pulse-echo beam profile of less than 0.5 mm has been maintained over a total depth range of 10 cm. An additional, though important, benefit is an observed reduction in the coherent speckle artefact, as compared with images obtained using conventional transducers. The prototype mirror system is limited in sensitivity (−15 dB relative to a highly focused transducer), noise due to mirror reverberations and a high side-lobe level (−11 dB worst case).

EARLY DETECTION OF BREAST CANCER: THE VALUE OF ULTRASOUND MAMMOGRAPHY

By B. J. Hackeloer, G. Lauth, B. Huneke, V. Duda and R. Buchholz

Universitäts Frauenklinik Marburg, West Germany

We report about 500 ultrasound examinations of the breast using a water-tank scanner (UI Octoson, Ausonics, Sydney, Australia). A very good tissue differentiation of the breast is caused by a special technique and a high resolution. It permits visualization of the entire breast without any tissue impression in contrast to conventional contact scanners. Beside normal images and benign results, typical findings in 101 malignancies are demonstrated ("shadowing", "christmas tree" sign) and its value discussed. All examinations are correlated with X-ray mammography, thermography, needle-biopsy and pathohistology.

The use of a real-time scanner as an additional aid in cyst puncture was also discussed.

ULTRASOUND EXAMINATION OF THE BREAST

By J. T. Ennis and M. Reilly

Department of Radiology, Mater Hospital, Dublin

The success of ultrasound in other soft tissue areas has encouraged the study of its potential in breast diagnosis and, although numerous technical advances have contributed to image quality, the diagnostic accuracy of breast ultrasound does not compare favourably with more established techniques, such as Xeromammography. Ultrasound of the breast is most useful as a complementary examination for elucidating problem cases in mammography.

The ultrasonic appearance of the breast in 63 patients is described and compared with Xeromammography. Classification of irregularities is by pattern recognition such as (a) shape of the lesion, (b) internal echoes, (c) boundary echoes, (d) posterior and lateral detail, (e) appearance of surrounding tissue.

The overall diagnostic accuracy compared well with other reported series. The limiting factors in achieving greater accuracy were discussed.

1. The probes commercially available are not adequately focused for water-bath scanning, resulting in a loss of lateral resolution and a dependence of echo size on beam shape.
2. The swept-gain function, which should compensate for attenuation in the tissue, can result in a distortion of echo sizes.
3. Much of the shadowing and enhancement signs important for diagnosis are best represented in a linear scan, but the curved surface of the breast causes a refraction artefact. Preliminary studies of this involved simple mathematical models of the breast and a computer program written to simulate or "mimic" the linear movement of the probe and graph on the CRT. It is apparent that even a small difference in the speeds of propagation of sound in the water-bath and tissue can result in significant contributions of registration error.

Forthcoming events

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Programme from: ICR81. c/o Brussels International Trade Fair, Parc des Expositions B-1020, Brussels, Belgium.

2nd International Conference on Visual Psychophysics and Medical Imaging

Brussels, July 2–3, 1981. Organizers: IEEE; Vrije Universiteit Brussel. The conference is scheduled adjoining the XVth International Congress of Radiology, June 24–July 1, also in Brussels.

Main topics: physics of medical imaging, basic visual mechanisms and visual perception, image processing and display in (bio)medicine, human factors and visual fatigue, observer performance, systems for psychovisual evaluation, relations between human and machine vision, automated analysis of (bio)medical images.

Information: Dr. J. Cornelis, Vrije Universiteit Brussel (Electronica), Pleinlaan 2, 1050 Brussels, Belgium.

First International Symposium on Minimal Invasive Cancer

Organized by the University Clinic of Obstetrics and Gynaecology, Graz, Austria, to be held at the Kongresshaus, Graz, July 1–4, 1981. Language: English. Main topics: cervix, vulva, endometrium, breast, oesophagus, stomach, large intestine, lung, thyroid, urinary bladder, prostate, larynx, oral cavity, skin, other organs. Enquiries: Interconvention, PO Box 105, A-1014, Vienna, Austria (phone (0222) 57 62 88). President: Prof. E. Burghardt; Secretary General, Dr. E. Holzer.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

Society of Nuclear Medicine Europe

19th Annual Congress

September 8–11, 1981. Information: President Dr. H. Rösler, Department of Nuclear Medicine, Inselspital, 3010 Bern, Switzerland.

International Symposium and Course on Abdominal Ultrasound

Turku, Finland, August 10–12, 1981, organized by the Radiological Society of Finland and the European Association of Radiology. Language: English. Guest speakers: C. R. Hill, H. H. Holm, M. Johnson, A. Kratochwil, C. Metreweli, E. H. Smith and F. Weill. Two "free communications" sessions, for which 10 minute papers are invited: abstracts to be submitted with registration. Technical exhibition and social programme. Information and registration: Oy Konfer Ab, Yliopistonkatu 29 c B, SF-20100 Turku 10, Finland.

Contrast Media. Fundamentals and Clinical Application

The Department of Diagnostic Radiology of the University of Rochester will offer a two-and-a-half day course on Contrast media: fundamentals and clinical application, September 21–23, 1981. The philosophy of this course is to review the fundamental chemical, physical, physiological, and toxicological properties of radiopaque media and to describe the relationship and importance of these properties to radiological application and diagnoses. The curriculum will provide a thorough introduction to contrast media for residents, Fellows, and junior faculty as well as a refresher course for the more experienced radiologist. The knowledge conveyed should be useful in the clinical setting and in the laboratory. For further information, contact Harry W. Fischer, M.D., Chairman, or Michael R. Violante, Ph.D., Course Director, Department of Radiology, PO Box 648, University of Rochester Medical Center, Rochester, New York 14642; phone (716) 275-2617.

Skeletal Radiology

The Eighth Refresher Course of the International Skeletal Society will be given in Madrid, Spain, September 25–27, 1981.

For further information, please write to: A. Bonakdarpour, M.D., Department of Diagnostic Radiology, Temple University Hospital, 3401 North Broad Street, Philadelphia, PA 19140, USA; or Prof. Dr. Friedrich W. Heuck, Zentrales Röntgeninstitut, Katharinen Hospital der Stadt Stuttgart, Kriegsbergstrasse 60, Stuttgart 1, Germany.

European Association of Radiology

II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

The Faculty of Radiologists of The Royal College of Surgeons in Ireland

21st Anniversary Meeting, Dublin, October 2–3, 1981: jointly with The British Institute of Radiologists, The Royal College of Radiologists, and The Royal Society of Medicine. Diagnostic and therapy sessions; topics to include radiology in renal failure and radiology of trauma. The BIR Presidential Address for 1981, "Chest radiology—guesswork or science?" will be given by Dr. D. H. Trapnell. Technical exhibition. Details: Miss A. Daly, Faculty of Radiologists, Royal College of Surgeons in Ireland, Stephen's Green, Dublin 2.

Symposium of Radiological Physicists

Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

Forthcoming events

The Short and Long Term Biological Consequences of Exposure to Radiation

Middlesex Hospital, London. Tuesday, October 13, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

The Radiological Imaging of Thyroid Disease

Wednesday November 18, 1981

This all-day meeting, organized by the BIR Nuclear Medicine Committee, will be held in London (venue to be announced). The meeting will cover all aspects of thyroid disease, including the use of isotopes. There will be some invited speakers but proffered papers are invited and should be sent to: Dr. John Frank, The Wessex Regional Department of Nuclear Medicine, Southampton General Hospital, Southampton SO9 4XY before August 31 1981.

British Medical Ultrasound Society

The 1981 Annual Meeting will be held on December 14–15 at the University of London Union, Malet Street, London WC1. Proffered papers are invited; abstracts should be sent to Dr. W. Hately, X-ray Department, London Hospital, Whitechapel, London E1 1BB to arrive not later than August 31 1981.

Symposium on Education and Training in Radiobiology

Dresden, May 12–15, 1982. Organized by the Gesellschaft für medizinische Radiologie der DDR, under the auspices of the European Society of Radiology. Languages: English, French and German. Registration by December 1, 1981; papers by August 15, 1981. Information: Professor R. Barke, Radiologische Klinik, DDR – 8019, Dresden, Fetscherstrasse 74.

Society for Radiological Protection

Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ. Abstracts to be received by July 15, 1981.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01-486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

5th South African International Radiological Congress

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas participants, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

Founding of a European Society for Therapeutic Radiology and Oncology, Milan, September 1980

For a long time the need has been felt by most radiotherapists for a society covering their specific field of interest, namely clinical oncology with special interest in radiation therapy. By the end of 1979 the initiative to start such a society was taken by a group of radiotherapists. The first call for members, which was circulated in the spring of 1980, generated a general enthusiasm, and over 90% of all people contacted have answered favourably to this request. Over 250 radiotherapists from all the countries in Western Europe became founding members of the new society. The founding meeting was held in Milan in September 1980, and was organized in association with a meeting of the Group of European Radiotherapists. More than 130 radiotherapists were present at the inaugural administrative meeting and at the subsequent scientific meeting, the subject of which was the combination of radiotherapy and chemotherapy.

The European Society for Therapeutic Radiology and Oncology (ESTRO) has educational and scientific objectives. It will concentrate its efforts on promoting the standards of cancer management by radiotherapy as well as by other means, by facilitating the exchange of information among radiotherapists and between radiotherapy and other oncological disciplines. The society will organize every year an open meeting on therapeutic radiology and oncology in which the multi-disciplinary approach in cancer management will be stressed by inviting representatives from other specialities to participate.

The meeting in Milan was organized by a provisional board consisting of Alberto Banfi (Milan), Klaas Breur (Amsterdam), Jerzy Einhorn (Stockholm), Michael Peckham (London), Maurice Tubiana (Villejuif) and Emmanuel van der Schueren (Leuven). Klaas Breur was elected president and Jerzy Einhorn president-elect of the society, as a result of a written ballot in the month before the meeting. The provisional board is to remain in office until June 1981, during which time it will organize general elections for a full board. Emmanuel van der Schueren is the Secretary of the Society.

All medical doctors whose principal activity is in the field of radiotherapy and oncology may become full members of the society. Physicists and biologists with their main activity in the field of radiotherapy may become associate members. A junior membership is available for residents in training for radiotherapy. By April 1981 the membership of the Society numbered almost 500.

In 1981 there will be a Business Meeting of the members during the ICR in Brussels. The first full meeting of the ESTRO will be held from June 28 to 30, 1982 in the Mechanical Engineering Department, Imperial College, South Kensington, London W.8.

Forms for application for membership of the society can be obtained from the Secretariat of the Society: Emmanuel van der Schueren, Department of Radiotherapy, Academisch Ziekenhuis St. Rafaël, Capucienenvoer 35, 3000 Leuven, Belgium.

Book reviews

The Embryogenesis of the Human Skull. An Anatomic and Radiographic Atlas. By Robert Shapiro and Franklin Robinson, pp. 101, 87 figs., 1980 (Harvard University Press, Cambridge, Mass.) £27·00.
ISBN 0-674-24790-6

This book is described by the publishers as "the basic normative standard reference for studies on developmental skeletal disorders of the head and neck". It concentrates on the development of the fetal calvaria excluding the bones of the face. The major part of the book consists of a series of photographs and radiographs of fetal skulls in different orientations. These were either dried or prepared by the Spalteholz method which is an old-established technique involving staining with alizarin and clearing the specimen, which is then photographed by transillumination. There are also photomicrographs of stained paraffin and celloidin sections. Some of the photographs and radiographs and all of the sections have accompanying line diagrams.

There is a short introduction consisting of a brief description of the development of the various bones of the calvaria which follows the account given in the standard anatomical texts. A short section on material and methods follows this with lists of 157 dried and Spalteholz specimens from New Haven, New York and Pittsburgh. Each of the specimens is identified by a number, and the sex, crown-rump length and weight is given, together with the estimated age in weeks taken from a standard table. The sectioned material is not listed. None of these specimens is ever referred to again and it is therefore not possible to see what relationship they have to the bulk of the atlas, because none of the photographs has a specimen number. The lists are therefore of little value to the serious student who might want to examine the material further. It is not clear that even one of the 20 or so skulls that are photographed is drawn from the listed skulls, or that the radiographed skulls are the same as the photographed ones that immediately precede them. In some cases it is possible to tell by inspection that this is not so. Skulls from Harvard Medical School are acknowledged, but again, these are not listed or mentioned further. None of the photographs except the first two has a size scale and the subsequent pictures are not to the same scale. There is no index.

All the line drawings have labels composed of initials only although there is plenty of space around each drawing for a full label. The list of abbreviations is at the back of the book, thus necessitating constant referral whenever one of the pictures is examined. Some of the labels are misleading. In the PA radiograph of a skull at full-term, a label "m" is pointing at a molar tooth in the lower jaw and this is an abbreviation for mandible in the list. A curious aberrant object is present in the photograph and drawing of the disarticulated skull on pages 54 and 55. It is labelled "to" and given as "tooth" in the glossary which it certainly is not. There is nothing of this size or shape in the fetal skeleton.

This book is described on the jacket as a "solid piece of research, executed with considerable esthetic and scholarly finesse and which will serve as a definitive study on an important aspect of human fetal development". Aesthetically it is pleasing because the photographs are beautiful but the rest of the description is sadly inaccurate. It is a pity that something much more was not made of the material.

J. L. SCHEUER.

Interpreting Dental Radiographs. By B. Beeching, pp. iii+150, 385 illus., 1980 (Update Books Ltd, London) £12·00.
ISBN 906141-20-6

No radiologist will be killed in the rush to report dental films and this lack of enthusiasm has been compounded by the lack of a clearly written basic textbook on the subject. It was with enthusiasm that I started to read this new book by a senior lecturer at Guy's Hospital Dental School since its small size, clear print and good layout on two columns to the page augured well. The book opens with normal anatomy and techniques for taking intra-oral films, and continues with chapters on developmental abnormalities, caries and periodontal disease, then trauma and on through periapical changes and resorption to cysts, neoplasms and abnormalities of the skull and jaws. The only major omission is any mention of radiation protection, but perhaps it could be argued that this subject is outside the limits of the book.

The author's style is pleasant and very readable and is supplemented by some good drawings and excellent labelling of radiographs, with lines leading from the radiograph to clear print at the side of the illustration. However, the reproduction of the radiographs is not so satisfactory. They are lacking in contrast and depth of tone so that there is often difficulty in seeing the indicated abnormality, as shown in the first film where dental amalgam can hardly be seen as a different density to that of the adjacent tooth. The author obviously recognizes this difficulty since many radiographs, notably in the section on fractures of the mandible, have had the lesion drawn on the radiograph so that the true lesion is no longer visible, even if it did show beforehand.

The final section on "osteodystrophies" suffers even more severely from these difficulties in radiographic reproduction culminating in the penultimate film which is a chest X-ray printed back to front and with three labels pointing to abnormalities that cannot be seen.

On balance this book is clearly written and provides a good introduction to dental anatomy and disease that at this price is worth having available in areas where radiologists in training can refer to it. I hope the publishers can find a better way of reproducing radiographs and will then produce a second edition.

W. D. JEANS.

Cardiovascular Nuclear Medicine. Current Methodology and Practice. By C. M. Freeman and M. D. Blaufox, pp. viii+290, 1980 (Grune & Stratton, New York) $37.50. ISBN 0-8089-1292-5

The editors of this book are also the editors of *Seminars in Nuclear Medicine*. The October 1979, January and April 1980 issues of this journal were concerned with cardiovascular nuclear medicine, and that compilation of invited reviews is now published separately under a hard cover. There has been little discernible change between the former and the latter so any library already subscribing to *Seminars in Nuclear Medicine* has no need of this book. Nevertheless the articles are authoratively written by some of the best workers in the field. These include Bachrach and Green on instrumentation and data processing for the evaluation of left ventricular function, Zaret on first pass studies, Strauss on eight years of gated blood-pool scanning, Maseri on myocardial blood flow, Treves on shunts, Willerson, Parkey and Bonte on pyrophosphate scintigraphy, Pohost on thallium 201 physiology and Wackers on its use in acute infarction. There is an interesting review of edge detection techniques by Wei Chang and colleagues who apply the methods already in use in industrial and military situations to the nuclear medicine problem. They conclude that in the end there is little to choose between the clinical results obtained with different techniques and that ease of programming is an important consideration in making a choice.

There are chapters on topics less well covered by standard texts of nuclear cardiology, including cardiac trauma, shunt detection with short-lived gases and the complementary roles of cardiac ultrasound and cardiovascular nuclear medicine. The era of phase analysis of first pass and equilibrium gated studies is too recent for this text. The layout of the book and the emphasis on essays rather than direct instruction is appealing and there are well over 1000 references cited. The book is reasonably comprehensive and competes well with the many other recent texts on this subject.

K. E. BRITTON.

Progress in Nuclear Medicine Vol. 6. Cardiovascular Nuclear Medicine. Ed. by A. Righetti and A. Donath, pp. 225, 1980 (Karger, Basel) Sw. fr. 148/DM. 177/$88.75. ISBN 3-8055-0618-X

This latest volume in the series *Progress in Nuclear Medicine* is devoted to cardiovascular studies. This has undoubtedly been the most rapidly growing area in nuclear medicine over the last five years; growth has stabilized but not stopped and much of it has become incorporated into routine clinical work and therefore a progress volume is timely.

In reviewing this volume the introduction says it all—"This book is no exception to the rule . . . that a book written by several authors is almost inevitably uneven in style, length and quality . . .". Rarely is this so obvious, however—from trivial chapters which could have been put together by a radiology trainee to an eloquent treatise on regional perfusion using ^{133}Xe, a technique which almost no one else uses, and references varying from between three and 98 for a whole chapter, often to no later than 1978. I cannot agree with them, however, when later in the introduction they say ". . . . unevenness seems a small price to pay for the amount of experience and expertise provided by the contributors . . .".

There is little more to be said: most of the contributors have written better, more up-to-date, reviews elsewhere; the omissions are legion, *e.g.*, only exercise stress is mentioned with gated blood pool; where are cold stimulation, isometric and drug studies? where is dipyridamole thallium for one-legged patients with angina? and there is no mention of single-photon emission tomography—7-pinhole, rotating or transverse. In short, this is a disappointing volume.

M. N. MAISEY.

Computerized Tomographic Scanners in Europe

Edited by Roger J. Berry

British Journal of Radiology
Supplement 15

Under the auspices of the Commission Informatique of the European Association of Radiology, a Workshop was held at the Headquarters of WHO, Geneva, from 28 to 30 March 1979 on 'The Use of Computerized Tomographic Scanners in Radiotherapy in Europe'. It was clear from the first that CT scanning would have a major impact on radiotherapy, but how and where? At this meeting 150 experts from 17 countries met to review, from a real background in clinical experience of using CT scanners in radiotherapy planning, the progress which had been made and the costs involved. CT scanning is not inexpensive, but the information provided is in many cases unique. Following a keynote address by Professor Brian Pullan of the University of Manchester outlining what is and is not likely to be possible in future in tumour imaging, the papers cover the practical use of CT scan information in assessing tumour volume, planning radiotherapy and following tumour response in the head and neck, the thorax and the abdomen. The linkage of CT information to radiotherapy treatment planning is discussed, and the way indicated towards true three dimensional radiotherapy planning. All the papers presented at the Meeting are included in abridged form as well as rapporteurs' reports of the discussions in each section.

Orders to:
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
Price £19·50
ISBN 0 905749 09 X

Proceedings of The British Medical Ultrasound Society. Twelfth Annual Meeting, Nottingham, December 1980. 540
Forthcoming events. 551
European Society for Therapeutic Radiology and Oncology. 552

Book reviews

Oncology supplement: scientific foundations of oncology 466
Endoscopic retrograde cholangiopancreatography 483
Trattato di senologia 491
Ultrasound of the pediatric abdomen and pelvis 495
Forensic fetal osteology 495
Single photon emission computed tomography (symposium) 504
Grenz rays: an illustrated guide 504
Radiation drug interactions in the treatment of cancer 516
Topical reviews in radiotherapy and oncology 516
Biology of ovarian neoplasia 536
Thermoluminescence dosimetry 539
The embryogenesis of the human skull 553
Interpreting dental radiographs 553
Progress in nuclear medicine 6. Cardiovascular nuclear medicine 554
Cardiovascular nuclear medicine. Current methodology and practice 554

High dose-rate after-loading in the treatment of cancer of the uterus

Edited by Thelma D. Bates and Roger J. Berry

British Journal of Radiology Special Report 17

For more than fifty years intracavitary irradiation has formed a major part of the treatment of cancer of the cervix and corpus uteri. In recent years high dose-rate remote after-loading devices have been developed which have removed all radiation hazards to medical and ancillary staff and other patients, but until now the question "Are the clinical results achieved by high dose-rate after-loading intracavitary treatment of carcinoma of the cervix and corpus uteri at least as good as those achievable by conventional low dose-rate intracavitary techniques?" had not been answered by adequate clinical experience. At a meeting held at The Middlesex Hospital Medical School, London from 10–12 April 1978, 86 participants and observers from 36 Hospital Centres in 15 countries gathered to discuss relevant physics and radiobiology studies and to pool their clinical experience in the use of high dose-rate after-loading devices. This volume presents brief versions of their 33 contributed papers and a distillation of the lively discussion which took place. Although the conclusions reached were necessarily cautious, lest future results not reflect those already achieved, those so far with remote high dose-rate after-loading appear to be in no way inferior to the results of traditional methods. In fact there are indications that high-dose fractionated intracavitary therapy may be associated with a lower incidence of normal tissue complications for a comparable level of achievement of tumour local control in cancer of the cervix and corpus uteri.

High dose-rate remote after-loading devices have the ability to treat very large numbers of patients, and have a particularly valuable contribution to make in the treatment of these distressingly common cancers in developing countries. This volume provides comprehensive views of clinical and radiobiological experience for those centres acquiring or considering high dose-rate after-loading equipment.

ISSN: 0306–2120
ISBN: 0–905749–07–3

Price £15

Orders to:
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
(01–935 6237) or through your bookseller.

VOL 54 NO 642 JUNE 1981

The British Journal of Radiology

Contents

Page

Review article. Heating techniques in hyperthermia. 443
J. W. Hand and Gail ter Haar

The detection of spinal pseudarthrosis in ankylosing spondylitis. 467
W. M. Park, D. G. Spencer, I. W. McCall, D. J. Ward, W. Watson Buchanan and W. H. Stephens

Juvenile hyaline fibromatosis. 473
D. A. Stringer and C. M. Hall

Renal function after high dose urography in patients with renal failure. 479
Judith A. W. Webb, R. H. Reznek, W. R. Cattell and I. Kelsey Fry

The effect of DDAVP on intravenous urography. 484
A. K. Dixon, Judith A. W. Webb, W. R. Cattell and I. Kelsey Fry

Changes in sizes and distensibility of the aging kidney. 488
M. McLachlan and P. Wasserman

Severe complications from partial splenic embolization in patients with liver failure 492
I. Vujic and J. W. Lauver

The herniographic appearance of direct inguinal hernias in adults. 496
O. Ekberg

Mean skeletal dose factors for beta-particle emitters in human bone. Part II: surface-seeking radionuclides. 500
F. W. Spiers, A. H. Beddoe and Joan R. Whitwell

The effect of dexamethasone on the radiation survival response and misonidazole-induced hypoxic-cell cytotoxicity in Chinese hamster cells V-79-753B *in vitro*. 505
Barbara C. Millar and Sally Jinks

Technical note. 512
  A communication system for the transmission of nuclear medicine images over standard telephone lines.
  J. R. Corfield, C. P. Wells, F. M. Hall, P. Vernon and D. N. Croft

Case reports. 517
  Léri's pleonosteosis.
  M. Friedman, B. M. Lawrence and D. G. Shaw
  Histoplasma duboisii infection of bone.
  E. M. Thompson, J. Ellert, L. L. W. Peters, A. Ajdukiewicz and D. Mabey
  Retropharyngeal bleeding in haemophilia.
  R. I. Markowitz and J. B. Mendel
  Renal opacification during intravenous urography in acute cortical necrosis (the nephrogram in cortical necrosis).
  N. B. Bowley
  Caroli's disease: its diagnosis with non-invasive methods.
  Y. Imai, T. Watanabe, Y. Kondo and F. Nakanishi

Short communications. 529
  Potentiation of the radiation response of hypoxic mammalian cells by *cis*-dichlorobis (isopropylamine) trans-dihydroxy platinum IV (CHIP).
  M. Laverick and A. H. W. Nias
  Induction of micronuclei by irradiation with neutrons produced from 600 MeV protons.
  I. Diehl-Marshall and M. Bianchi
  Effects of dose fractionation after irradiation with neutrons produced by 600 MeV protons.
  M. Bianchi and I. Diehl-Marshall
  Long-term observation of mouse foot reaction after hyperthermia: hyperthermia may or may not be carcinogenic?
  M. Urano

Correspondence. 537
  Excretion of metrizamide in milk.
  K. F. Ilett, L. P. Hackett, J. W. Paterson and C. C. McCormick
  Strategic marking in MCQ papers.
  P. J. Robinson
  Ultrasonic measurement of the lumbar spinal canal.
  H. R. Stockdale and D. Finlay

(*continued on inside back cover*)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by The British Institute of Radiology
32 Welbeck Street, London W1M 7PG

ISSN 0007-1285
16633